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INITIAL AEROBIC FLORA OF NEWBORN (PREMATURE) INFANTS

NATURE, SOURCE AND RELATION TO ULTRAVIOLET IRRADIATION AND FACE MASKS

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A number of studies published within the past twenty years report the initial flora of the upper respiratory tracts of newborn infants. There is general agreement with respect to the bacterial types constituting the basal flora but a difference of opinion as regards their derivation and the presence of such pathogens as the beta hemolytic streptococci, the pneumococci and the influenza bacillus.

This investigation [1] was undertaken to clarify the latter point and to determine more definitely the sources of the initial flora and the modes of transmission to the respiratory tracts of newborn infants. The sterility or near sterility of this region in the majority of infants at birth simplifies the conditions of such a study of transmission by contact. The environmental conditions also permitted observations on the influence of ultraviolet irradiation of the air of a room on the initial flora. This study differs further from previous ones in the same field in that the infants were all either premature or underweight and were all artificially fed. They were cared for under the exacting conditions of aseptic nursing technic considered particularly important for infants of this type, and the number of contacts with adults was strictly limited.

SUBJECTS AND METHODS

The infants, with few exceptions, were born in the obstetric division of New York Hospital and were admitted, generally within one to two hours, to the unit for premature infants in the pediatric division. Cultures were made from the nasopharynges and throats of over 150 babies. As often as was feasible, specimens were taken on the first, second, third or fourth day of life and subsequently at irregular intervals until discharge, which usually occurred in three to four weeks.

During the early work specimens were obtained from the nasopharynx alone by passing fine cotton swabs on flexible copper wire through each nasal passage. The swabs were placed in test tubes containing 2 cc. of "hormone" blood broth (p_H 7.5), delivered at once to the laboratory and seeded on suitable culture mediums, for the most part blood (rabbit) "hormone" agar and ascitic fluid "hormone" agar (p_H 7.5). The plates and tubes were incubated at 35 C., and further plates were inoculated from the latter when it was deemed advisable. If delay in planting was unavoidable the specimens were kept in the refrigerator. Later in the study specimens for culture were also obtained from the throat and the rectal region. In addition, nasopharyngeal and pharyngeal cultures were made at intervals from all personnel in contact with the babies, including physicians, nurses and attendants. Representative colonies were fished from the plates into tubes of semisolid hormone agar and identified by appropriate procedures.

Environmental Conditions.—The infants were housed in four small nonconnecting wards without cubicle partitioning, each containing six bassinets. Two were identical and air conditioned for a temperature of 80 F. and a relative humidity of 65 per cent with fifteen changes of air per hour. The other two wards were similar but not air conditioned. Germicidal ultraviolet lights were installed in one of each pair of rooms with and without air conditioning. Accordingly, one room was without air treatment, one with air conditioning alone, one with ultraviolet irradiation alone and one with ultraviolet irradiation and air conditioning. The ultraviolet rays are generated by 36 inch General Electric 30 watt lamps with a radiation having a maximum wavelength of 2,537 angstrom units, the optimal for germicidal action. The lamps, six for each of the two wards of 3,630 to 4,840 cubic feet of air space, were placed on the walls 8 feet (2.5 meters) above the floor and 3 feet (1 meter) below the ceiling, and they were provided with baffles to protect the eyes by deflecting the rays from the line of vision in the horizontal plane. This arrangement obviated the need for protective eye glasses. The lamps were operated continuously, and after more than a year there was no indication of any ill effect on the infants or those in attendance. Although only the air of the upper part of the room received direct irradiation, effective germicidal action as shown by cultures was obtained for the air in all parts of the room. In fact, the amount of irradiation exceeded that which Wells and Wells [2] estimated as equivalent in purification of the air to one hundred changes per hour. Admission to these wards was limited to the assigned staff of doctors, nurses and attendants, who were required at all times to wear a conventional gauze or butter cloth mask. Thorough scrubbing of the hands was routinely performed between the handlings of different infants.

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1. The study was suggested by Dr. Samuel Z. Levine. Mrs. May H. Salinger and Mrs. Eleanor H. Stickney gave volunteer technical assistance.

2. Wells, W. F., and Wells, M. W.: Measurement of Sanitary Ventilation, Am. J. Pub. Health **28**:343 (March) 1938.

Table 1 gives representative bacteriologic analyses of the air of these wards from samples obtained with an air centrifuge and from exposed culture plates. The Wells air centrifuge [3] was designed to give information relating to the number and types of bacteria floating in the air as "droplet nuclei," namely the residue, after evaporation, of the finer droplets ejected from the mouth and nose in coughing, sneezing and to a lesser extent in talking. Each sample of air circulated amounted to 10 cubic feet (0.283 cubic meters). The blood agar plates, 10 cm. in diameter, were exposed for two hours at an elevation of approximately 3 feet (1 meter) from the floor, shaded from the direct rays of the lamps. They give information relating to bacteria attached to particles heavy enough to sediment. Routine activities were not interrupted during sampling.

The comparative results revealed that ultraviolet irradiation was accompanied by a reduction of 75 to 80 per cent, by elimination of streptococci and by practical disappearance of hemolytic strains of Staphylococcus aureus. The presumption is, therefore, that infants in the irradiated wards do not acquire bacteria of either of these types from the air. This conclusion received substantiation from tests of numerous additional samples of the air. Air conditioning alone seemed to effect in these particular samplings a 40 to 50 per cent bacterial reduction, although the results of tests for the ward so supplied were less consistent than those for the wards provided with ultraviolet irradiation. The bactericidal potency of ultraviolet radiation as estimated from these results, exceeds that reported by Brooks, Wilson and Blackfan [4] in the wards of the Boston Infants Hospital. Whereas their average ratio for bacteriologic counts in the irradiated and the non-irradiated wards was 1:2.5, ours was about 1:5. Furthermore, they noted no effect on the Staph. aureus content of the air, whereas in our experience this organism was practically eliminated from the air by irradiation.

TABLE 1.—*Bacterial Content of Air (March and December Samplings Combined)*

Ward	Number of Infants	Treatment of Air	Samples		Average Number of Colonies per Sample		
			Nature	No.	Total	Staph. aureus (Hemolytic)	Str. (Alpha)
Premature	6	Ultraviolet irradiation and air conditioning	Centrifuge *	5	12	0.0	0.0
			Plates †	7	14	0.14	0.0
Premature	2 to 4	Ultraviolet irradiation	Centrifuge	5	14	0.0	0.0
			Plates	7	15	0.0	0.0
Premature	4 to 6	Air conditioning	Centrifuge	5	36	0.4	0.0
			Plates	5	25	0.6	0.0
Premature	4	None	Centrifuge	4	61	1.0	1.0
			Plates	7	56	2.0	1.0
Sick infant (for comparison)	6	None	Centrifuge	3	48	1.0	0.0
			Plates	10	77	1.8	1.0

* Air centrifuge sample, 10 cu. ft.

† Blood agar plates, exposed to air 2 hours.

ULTRAVIOLET IRRADIATION IN RELATION TO THE INITIAL RESPIRATORY FLORA OF NEWBORN INFANTS

Previous investigators have differed widely in their reports on the aerobic bacteria of the upper portion of the respiratory tracts of infants immediately following birth. Kneeland [5] observed that for 80 per cent of the infants tested throat cultures taken within a few hours of birth (platings) yielded no growth. On the other hand, Witkowski [6] reported that the oral cavity was sterile in only 2 per cent of 50 infants for whom cultures were made shortly after birth. Bloomfield [7] found sterility in all of 18 infants tested, whereas Gundel and Schwarz [8] for 40 infants tested within six hours of birth reported the mouth as sterile in 37.5 per cent and the nose in 42.5 per cent. Schweitzer [9] obtained growth in 46 per cent of a series of cultures taken from the mouth immediately after birth. These differences seem largely referable to the methods used. Kneeland made platings directly from the swabs, whereas Gundel and Schwarz and also Witkowski incubated a broth tube seeded from the swab and plated from this at the end of four and twenty-four hours respectively. Further, in the latter two studies swabbings were made from the whole oral cavity, not from the throat alone. Our technic was similar to that of Kneeland, and in cultures from the throats and nasopharynges of 16 infants within sixteen hours after birth we found, as he did, indications of a sterile condition in 80 per cent. The incidence of oral sterility was practically the same for infants in and out of the ultraviolet-irradiated wards, 87 and 75 per cent respectively. Infants 24 hours old and less than 48 hours yielded

3. Wells, W. F.: Air-Borne Infection: I. Apparatus for the Study of Bacterial Behavior of Air, Am. J. Pub. Health **23**:58 (Jan.) 1933.

4. Brooks, G. L.; Wilson, U., and Blackfan, K. D.: Studies in Cross Infection in the Infants' Hospital of Boston, in Aerobiology, Publication 17, American Association for the Advancement of Science, 1942, p. 228.

5. Kneeland, Y., Jr.: Studies on the Common Cold: III. The Upper Respiratory Flora of Infants, J. Exper. Med. **51**:617 (April) 1930.

6. Witkowski, R.: Aerobe Mundhöhlen Flora bei Mutter und Kind, Zentralbl. f. Bakt. (Abt. 1) **133**:334 (Feb.) 1935.

7. Bloomfield, A. L.: Adaptation of Bacteria to Growth on Human Mucous Membranes, with Special Reference to the Throat Flora of Infants, Bull. Johns Hopkins Hosp. **33**:61 (Feb.) 1922.

8. Gundel, M. W., and Schwarz, F. K. T.: Studien über die Bacterienflora der oberen Atmungswege Neugeborener, Ztschr. f. Hyg. u. Infektionskr. **113**: 411, 1932.

9. Schweitzer, B.: Ueber die Entstehung der genital Flora, Zentralbl. f. Gynäk. **43**:614, 1919.

sterile cultures in 50 and 12.5 per cent respectively in the irradiated and nonirradiated wards (table 2). The evidence suggested that ultraviolet irradiation delayed to some extent the acquisition of the initial flora. From the age of 48 hours on, the throats of all the infants yielded positive cultures. There was clear evidence that the primary bacteria first invaded the infant through the mouth and not the nose, as positive cultures were often obtained from the throat twelve hours or more before the nasopharynx yielded growth; in fact, the latter region might remain sterile or nearly so up to four days after birth.

Comparing further the figures given in table 2, it may be noted that in this particular series, which included pharyngeal cultures, alpha streptococci and to a lesser degree Staph. aureus were acquired somewhat later by infants in the irradiated than in the nonirradiated wards. The irradiated rooms. In this series there was no significant difference as regards the streptococci; if anything the infants in the irradiated wards had a slightly higher percentage of positive cultures during the first ten days of life. In the absence of viable streptococci in the irradiated air, it may be concluded, as will be shown later, that these organisms were largely transmitted directly from the respiratory tracts of the adults in contact with the infants, despite the use of masks.

The only observation suggesting that ultraviolet irradiation might have been a modifying influence on the flora of the infants in this series was the somewhat later occurrence of Staph. aureus on the nasopharynx (table 3). Its prevalence in the air of the nonirradiated rooms and its scarcity in the irradiated air indicated that the infection might have been to some extent air borne in the former.

TABLE 2.—*Bacterial Content of Cultures from Nasopharynx and Throat (Combined) for Newborn Infants Exposed and Not Exposed to Ultraviolet Irradiation*

Age at Time of Test	No. of Infants	Staph. Albus		Str. (Alpha)		Str. (Gamma)		Staph. Aureus (Hemolytic)		Diphtheroids		Esch. Coli		G— Rods Aerobic		G+ Large Cocci		Sterile	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
No Ultraviolet Irradiation																			
Up to 16 hr.	8	1	12	1	12	0	0	0	0	0	0	0	0	1	12	0	0	6	75
1 day.....	16	10	62	9	56	0	0	0	0	0	0	1	6	4	25	4	25	2	12
2-4 days....	22	16	73	15	68	7	32	7	32	4	18	2	9	8	37	8	37	0	0
5-25 days...	16	12	75	16	100	10	62	10	62	1	6	4	25	2	12	1	6	0	0
Ultraviolet Irradiation																			
Up to 16 hr.	8	0	0	0	0	0	0	0	0	0	0	1	12	0	0	0	0	7	87
1 day.....	12	5	42	2	17	0	0	1	8	1	8	2	17	1	8	0	0	6	50
2-4 days....	13	8	62	5	38	3	23	2	15	0	0	3	23	2	15	7	54	0	0
5-25 days...	11	6	54	9	82	1	9	6	54	2	18	4	36	0	0	3	27	0	0

term "gram-negative rods (aerobic)" (table 2) refers to an unidentified nonspore-bearing organism, coliform in structure and type of colony but strictly aerobic. It formed no gas in dextrose broth, fermented lactose feebly and did not liquefy gelatin. It occurred irregularly. Other transitory and irregularly occurring organisms were Escherichia coli, diphtheroids, large gram-positive cocci and the gamma or indifferent streptococci. Under the name Staphylococcus albus are included various species of nonhemolytic micrococci forming white colonies. By far the most frequent was Staphylococcus epidermidis, less frequent was Micrococcus candidus. A hemolytic strain of Staph. albus was rarely noted. These white cocci occurred early in the flora and were often predominant.

Constant components of the flora were certain types of nonhemolytic streptococci and hemolytic Staph. aureus. In the early work cultures were made from the nasopharynx alone, and table 3 presents the incidence of these organisms in that location for infants in the irradiated and the non-

Our results on premature and immature infants are compared in table 4 with those reported by Kneeland [5] for presumably normal infants of

TABLE 3.—*Occurrence of Nonhemolytic Streptococci and Hemolytic Staphylococci in Nasopharynx*

Age in Days	No Ultraviolet Irradiation			Ultraviolet Irradiation		
	No. of Infants	Positive		No. of Infants	Positive	
		No.	%		No.	%
Streptococcus (Alpha or Gamma)						
1	35	10	29	31	12	39
2-3	33	22	67	21	17	81
4-10	34	27	80	23	21	91
Staph. Aureus (Hemolyticus)						
1	33	3	9	25	2	8
2	20	3	15	17	2	12
3	18	8	44	15	4	27
4-6	28	12	43	24	6	25
7-25	56	33	60	28	12	43

the same age. The only noteworthy differences are the higher incidence of Staph. albus, the lower incidence of green streptococci in the nasal cultures of Kneeland and perhaps the difference in the ratio of the two types of streptococci in

the throat. The first of these differences is probably explained by the fact that our specimens were not strictly nasal but included nasopharyngeal material. The difference in the reported percentages of the green and indifferent streptococci in cultures from the throat may perhaps be referable to differences in methods of classification, our differentiation being based on the observation of subsurface growth of each isolated streptococcus strain in blood agar. Not infrequently transplants from a surface colony of the gamma type on the primary culture plates produce a green discoloration of the medium when so tested.

INCIDENCE OF PATHOGENS IN THE FLORA OF NEWBORN INFANTS

Table 5 shows the incidences, in percentage, of various organisms [10] in the nasopharynx during the first ten days of life, with and without ultraviolet irradiation of the air.

No noteworthy differences were observed with and without treatment of the air. Of particular interest is the complete or almost complete absence of such pathogens as beta hemolytic streptococci, pneumococci, Friedländer's bacillus and representatives of the influenza group in both groups of infants. These results are in accord with the observations of Kneeland [5] and of Bloomfield [7] for infants during the first two weeks of life. On the other hand, they differ from the results reported by Gundel and Schwarz [8] and by Witkowski [6] for cultures from the throats of newborn breast-fed infants. Gundel and Schwarz, in cultures from 52 infants made during the first twelve days of life, found Hemophilus influenzae in 12 per cent, hemolytic streptococci in 63 per cent, pneumococci in 59 per cent and Friedländer's bacillus in 8 per cent. Similarly Witkowski, for 50 infants during the first five days of life reported an incidence of 14 per cent for hemolytic streptococci and 46 per cent for pneumococci. Both investigators concluded that these pathogens were transmitted from the mothers, since they were present in the maternal pharyngeal flora in similar percentages, and contact with the infants was naturally close. Neither article gives information concerning the number or persistence of these pathogens. In this study, special precautions were taken to prevent contact with carriers of such pathogens. As a matter of hospital routine, cultures are made from the throats of the doctors, nurses and others participating in the infants' care, and known carriers are excluded. It is, however, practically impossible to prevent such contacts entirely, and additional cultures taken from the personnel indicated that the infants were at times exposed to carriers of pathogens. Thus, beta hemolytic streptococci were found in the throats of 5 adult contacts; pneumococci, including types III, XIX, XXII and XXIII, in 7; H. influenzae, in 3 on the same date, and Friedländer's bacillus, in 2. Nonpathogenic hemoglobinophilic organisms, such as Haemophilus haemolyticus, were frequently present in the adults as were gram-negative diplococci, yet neither these nor the listed pathogens were implanted in the upper respiratory tracts of the infants.

TABLE 4.—*Organisms Predominating in First Positive Cultures From Nasopharynx and Throat (No Ultraviolet Irradiation.)*

Location	No. of Infants	Str. (Green) %	Str. (Indifferent) %	Staph. Albus %	Staph. Aureus %	Colon Group %	Diphtheroid Group %	Large G + Cocci %
Present Series; Newborn Subnormal Infants								
Nasopharynx (Jan.-Dec. 1942)	52	31	8	46	8	2	0	6
Nasopharynx (Jan.-June 1943)	23	39	0	22	22	9	0	9
Throat (Jan.-June 1943)	24	46	4	38	8	0	0	4
Kneeland's Series (1930); Unselected Newborn Infants								
Nasal passages	25	4	4	76	8	0	4	4
Throat	30	37	23	27	3	3	3	3

TABLE 5.—*Percentage of Incidence of Organisms in Nasopharynx in Infants up to Ten Days of Age*

Treatment of Air	No. of Infants	Str. (Green)	Str. (Indifferent)	Staph. Albus	Staph. Aureus	Colon Group	Diphtheroids	Large G + Cocci	G — Cocci	Str. (Hemolytic)	Proteus	Hemoglobinophilic Group	Pneumococci
Ultraviolet irradiation	25	80	40	72	40	4	4	12	4	0	0	4	0
No ultraviolet irradiation	37	76	41	84	49	14	19	27	5	3	3	0	0

10. Representatives of the Lactobacillus group were not studied, but they were undoubtedly present, since Witkowski [6] and others have reported an incidence of 48 per cent in the mouths of newborn infants.

Bloomfield [7] in his study of the flora of the throats of newborn infants, suggested that "any organism which persists on a normal mucous membrane for more than a few hours must have a biological relationship to the mucous membrane; otherwise it would be removed as a foreign particle by the normal eliminative mechanism." In conformity with this theory, we tentatively suggest that the apparent relative freedom from infection with these bacterial types in newborn infants is not due so much to an inherited specific immunity in the child as to a relative lack of biologic adaptation of the bacterial organism to the immature tissues of the infant's nose and throat.

Observations on the relative persistence of various fermentative types of streptococci on the respiratory mucous membranes of newborn infants lend further support to this theory. Throughout this investigation representatives of all types of colonies of streptococci appearing on the culture plates were fished into tubes of semisolid "hormone" agar and fermentation tests were made from these subcultures. The basal medium was the same as designated in a previous article by one of us,[11] except that 0.1 per cent agar was added. The carbohydrates tested were present in 0.5 per cent amounts. In table 6, the nonhemolytic streptococci are grouped on the basis of the fermentation of lactose, salicin, mannitol and raffinose after four to five days' incubation. The figures show the percentage of persons yielding cultures positive for each group. In the throats of adults the forms which ferment raffinose occurred most frequently (in 63 per cent of 40 persons); the next in frequency were the strains which split lactose but none of the other three carbohydrates. The latter type was the one most frequently recovered in the first positive cultures from exposed infants, although representatives of all the types which occurred in the adults were present in the 1 to 4 day old infants and in somewhat similar percentages. In cultures taken at the age of 2 to 4 weeks, this type, which fermented lactose but not salicin, mannitol or raffinose remained strongly prevalent with the type which fermented lactose and salicin but not mannitol or raffinose next in frequency. The raffinose-fermenting types now were rarely encountered.

Sherman, Niven and Smiley,[12] in their recent definition of Streptococcus salivarius, state that fermentation of salicin and raffinose is a constant characteristic of the species. Although no other species-differentiating tests were made, it seems probable that the figures in column d, table 6, represent largely strains of Str. salivarius and that this species cannot adjust itself to the mucous membranes of the newborn infant's throat. A similar lack of adjustment would seem to exist for the fermenters of mannitol and to a lesser degree for the strains fermenting none of the carbohydrates. The other types capable of adaptation were probably strains of Streptococcus mitis (fermenting lactose and salicin). By analogy, this demonstrated selective adaptation suggests that pneumococci, hemolytic streptococci and the hemoglobinophilic bacteria may likewise not find as favorable soil for growth and persistence in newborn infants as in older persons. In fact, Kneeland first noted the appearance of these pathogens in infants who had reached the age of 2 to 4 months. Against this theory are the reports of Gundel and Schwarz and also Witkowski that pneumococci, hemolytic streptococci and H. influenzae may be present in the oral cavity of newborn infants. However, they submitted no evidence that these pathogens were more than a transient element of the flora. Even though newborn infants may be safeguarded to some extent by this factor, the occasional case of pneumococcic pneumonia or bacteremia shows that this natural protection, if it exists, is by no means complete.

TABLE 6.—*Selective Adaptation of Streptococci to the Upper Respiratory Tract of Newborn Infants*

			Alpha or Gamma Streptococci, Fermentative Types				
			a	*b*	*c*	*d*	*e*
			Lactose —	Lactose +	Lactose +	Lactose + +	Lactose + +
			Salicin —	Salicin —	Salicin +	Salicin — +	Salicin + +
			Mannitol —	Mannitol —	Mannitol —	Mannitol — or —	Mannitol + or +
			Raffinose —	Raffinose —	Raffinose —	Raffinose + +	Raffinose — +
Source	No. of Cases	Region	% Positive	% Positive	% Positive	% Positive	% Positive
Adult contacts	40	Throat	35	50	38	63	13
Infants (mostly 1-4 days old) first positive culture	43	Nasopharynx and throat	21	51	19	33	7
Infants (2-4 weeks old) last cultures	22	Nasopharynx and throat	9	68	36	5	0

11. Torrey, J. C., and Lake, M.: Streptococci in Air as an Indicator of Nasopharyngeal Contamination, J. A. M. A. **117**:1425 (Oct. 25) 1941.

12. Sherman, J. M.; Niven, C. F., Jr., and Smiley, K. L.: Streptococcus Salivarius and Other Non-Hemolytic Streptococci of the Human Throat, J. Bact. **45**:249 (March) 1943.

SOURCES AND MODES OF TRANSMISSION OF THE RESPIRATORY FLORA OF NEWBORN INFANTS

Previous investigators are not agreed on the relative importance of the various sources from which the initial nasopharyngeal flora of the infant is derived. Salomon [13] and Witkowski [6] concluded that the "banal" flora is acquired during birth from the vaginal region of the mother, whereas Gundel and Schwarz [8] did not consider this source or the mother's breast or the hands of attendants of primary importance, but rather the oral flora of those in contact. Kneeland [5] merely states that the first positive cultures were obtained after the first feeding and Bloomfield [7] that the staphylococci of the nursing infant's flora were clearly derived from the mother's skin and milk. None of these opinions were supported by convincing bacteriologic evidence.

The parturient canal is an obvious source from which bacteria might be acquired by newborn infants, whether subsequently breast fed or bottle fed. Accordingly, vaginal cultures were made during the first stage of labor from twenty consecutive patients in the obstetric division of New York Hospital.[14] The material was taken up on swabs and placed in tubes containing a small amount of nutrient broth. Platings were made both directly from the swab and from the broth after twenty-four hours' incubation. The mediums included ascitic fluid "hormone" agar, tryptose dextrose-blood agar and eosin–methylene blue agar, all with a p_H of 7.2 to 7.4. In table 7 are listed the percentages of cases in this series in which each of the aerobic organisms occurred. The bacterial types observed and their relative numbers are in general similar to those reported by Weinstein [15] in his extensive study of the bacteriology of the human vagina. Differences in the percentages are probably ascribable to the fact that specimens were taken less deeply in the vagina in our patients.

Before discussing the significance of the vagina as a source of each component of the newborn infant's respiratory flora, it may be said in general that we do not believe it is by any means so important as claimed by Salomon and by Witkowski; such part as it may play is of course influenced by the duration of labor and probably by the time of rupture of the amniotic membranes. In this connection an apparently unique and clearly defined implantation from the vagina is reported. Cultures taken from the throat and nasopharynx of a Negro infant [16] sixteen hours after birth yielded a pure growth of gonococci from each site, with the heavier growth from the throat. On the second day the gonococci had disappeared and were replaced by white staphylococci. Two weeks later the mother was recalled to the hospital, and from the cervix and urethra the laboratory service of the obstetric division isolated a strain of gonococci identical in all respects with that recovered from the infant.

Without doubt several types of organisms may be implanted in the oral cavity during birth, but we found that in general they were transient invaders, whereas the types that persisted were derived largely from the noses and throats of adults who were in contact with the infant. In the following sections various possible sources of implantation (vagina, mouth droplets, fingers of those in contact and air) are considered in connection with each group of bacteria. The food may be dismissed as a possible vehicle, as it was nearly sterile and such bacteria as were present in it were foreign to the oral flora.

TABLE 7.—*Aerobic Organisms in Cultures from Vaginal Region Just Prior to Labor (Percentages of Mothers with Positive Cultures)*

No. of Cases	Staph. Albus	Staph. Aureus	Str. (Alpha or Gamma)	Str. (Beta)	Esch. Coli	Diphtheroids	Lactobacillus	Yeasts
20	100	0	50	0	40	55	35	15

Streptococci.—It apparently was assumed by Salomon [13] and Witkowski [6] that the nonhemolytic streptococci of the vagina and those capable of adjustment to the respiratory mucous membranes of the newborn are the same. That this view is largely erroneous is indicated by the distribution of fermentative types as shown in table 8; the fermentative type best able to adjust to the infant throat (fermenting lactose but not salicin, mannitol or raffinose) was not represented among the vaginal strains. On the other hand, the mannitol-fermenting strains, which constituted nearly one fourth of the vaginal streptococci, were rarely present in the initial cultures from infants, and in the few instances in which they were acquired they did not persist.

Another possible source of streptococci was the fingers of the caretakers. In exploring this possibility, cultures from the fingers of the nurses were made by having them impress

13. Salomon, R.: Die Entstehung der genital Flora: II. Die Entstehung der Mundkeime, Ztschr. f. Geburtsch. u. Gynäk. **85**:306 (Oct.) 1923.

14. Dr. William F. Finn assisted us in obtaining the specimens.

15. Weinstein, L.: Bacterial Flora of the Human Vagina, Yale J. Biol. & Med. **10**:247 (Jan.) 1938.

16. Dr. R. Gordon Douglas, of the department of obstetrics, cooperated in the study of this case.

lightly the balls of all fingers on plates of ascitic fluid agar. This procedure was more effective than swabbing the fingers and then seeding culture plates. In thirteen impression tests made during the care of an infant streptococci were obtained five times, but after routine scrubbing of the hands before caring for another infant positive cultures were obtained only twice and then only to the extent of a few colonies from one or two fingers. These results indicated that transmission on fingers was no more than a minor factor in the infant's acquisition of streptococci. Transmission by air would seem to be eliminated as an important factor since streptococci were acquired as quickly (by up to 80 per cent of the infants in two to three days) in the wards with air freed of them by ultraviolet irradiation as in those with air not so treated.

The foregoing considerations pointed to direct contact transmission from adult to infant through droplets of saliva as the mode of primary importance. If this conclusion is correct, it indicates that droplets were at times projected through the face masks in the absence of coughing and sneezing. As this hypothesis has such a direct bearing on the question of the efficacy of masks as a protective device in wards for infants, we endeavored to trace streptococci recovered in the initial positive culture from the throat or nasopharynx of an infant to a particular nurse or doctor. Platings were made from the throats and nasopharynges of all adults in contact with the infant, and the characteristics of all the strains of streptococci were determined, including detailed structure of the colony, exact reaction on blood agar, structure of the organism, character of growth and oxygen requirements as indicated in stab cultures in semisolid hormone agar and results of fermentation tests. The same data were determined for the first strains of streptococci recovered from infants, generally on the first or second day of life. In a number of instances matching was complete between a strain from a particular doctor or nurse and that from the infant and not for the strain from any other known contact. For 3 infants the identity of the strains as indicated by these comparisons was substantiated by agglutination tests.

A baby was admitted to the ultraviolet-irradiated ward for premature infants immediately after birth at 10:55 p. m., Oct. 16, 1942. Contact occurred with two doctors and two nurses soon after admission but with no others until the next morning. Twelve hours after these first contacts, cultures were made from material from the nasopharynx of the infant; on blood agar a few rough, papillated colonies of alpha prime streptococci developed and nothing else. This strain fermented lactose but not salicin, mannitol or raffinose, and it was thus foreign to the vagina according to our observations. Of the four adults in contact doctor X was the only one who harbored in the throat a strain of streptococci morphologically and culturally identical with the one in the infant. A rabbit was immunized to this (X) strain, and agglutination tests were conducted by the method described by Mueller and Klise.[17] The titer for the homologous strain was 3,200, and for the strain from the infant, 1,600. In view of the well known tendency toward serologic heterogeneity in strains of alpha streptococci, this strong cross agglutination is particularly indicative of identity. Hooker and Anderson[18] observed strong cross agglutination in less than 3 per cent of six hundred and sixteen tests with alpha streptococci. On the other hand, Sherman, Niven and Smiley[12] recently stated that about 40 per cent of the strains of Str. salivarius which they tested belonged in one agglutinative unit. However, the strains for which we claim identity were not Str. salivarius. Further agglutination tests indicated that at the same time this physician transmitted the alpha prime streptococci to 2 other infants with whom he had been in contact shortly after their birth. From the nasopharynx of an infant 8 hours old and of another 2 days old were recovered alpha prime streptococci identical culturally and morphologically with the strain from the physician. The strains from the infants agglutinated to the full titer of the serum, (3,200).

TABLE 8.—*Comparative Distribution of Fermentative Types of Nonhemolytic Streptococci in Flora of Maternal Vagina and of Throat and Nasopharynx of Newborn Infants*

			Types				
			a	*b*	*c*	*d*	*e*
			Lactose —	+	+	+ +	+ +
			Salicin —	—	+	— +	+ +
			Mannitol —	—	—	— or —	+ or +
			Raffinose —	—	—	+ +	— +
Sources	Region	No. of Cases	Percentage of Cultures Positive				
Infants 1 to 4 days old.....	Nasopharynx and throat	43	21	51	19	33	7
Women prior to labor.....	Vagina	10	31	0	31	15	23

Staphylococci.—Nonhemolytic white staphylococci are generally the organisms first to appear in the throat and nasopharynx in newborn infants. They are so ubiquitous that they may well be acquired from a number of sources, such as

17. Mueller, J. H., and Klise, K. S.: A Method for the Agglutination of Hemolytic Streptococci, J. Immunol. **22**:53 (Jan.) 1932.

18. Hooker, S. B., and Anderson, L. M.: Heterogeneity of Streptococci Isolated from Sputum, J. Immunol. **16**:291 (April) 1929.

the vaginas, the oral cavities and the fingers of adults and the air. As they seem to be of no clinical importance, no effort was made to trace their source in specific instances. On the other hand, the hemolytic coagulase-positive strain of Staph. aureus is a potential pathogen, despite its frequency in the nose and throat of infants and the relative rarity of developing infections. Although the portal of entry seems to be the mouth rather than the nose, more favorable soil for its growth is provided by the nasopharynx than the throat. It not infrequently is the predominant organism in the nasopharynx in 1 to 3 week old infants. Contrary to Bloomfield's [7] opinion that it is transient, we have found that once implanted on the nasopharynx of an infant it tends to persist. In 1 case a strain of Staph. aureus acquired on the second day of life was recovered on the fiftieth day and was apparently the cause of otitis media, as the initial and the later strain isolated from the nasopharynx and that isolated from the ear were culturally and serologically identical. In other infants persistence of the initially acquired strain for at least two to three weeks was demonstrated. Of a total of ninety-eight strains isolated from these infants, eighty-five (86 per cent) tested strongly positive for coagulase and thus were presumably potential pathogens. The usual technic was followed in performing this test, suspending one loop of a twenty-four hour growth from an agar slant in 0.5 cc. of rabbit plasma diluted once with isotonic solution of sodium chloride. Readings were made after incubation for three hours at 35 C. As shown in table 3, 60 per cent of infants from 7 to 25 days old in the nonirradiated wards had acquired pathogenic strains of Staph. aureus. This is approximately the same as the 58.4 per cent incidence of coagulase-positive Staph. aureus reported by Hallman [19] for the anterior nares of 272 children from 2 months to 12 years old and as the 64.5 per cent of carriers among subjects tested in the Infant's Hospital in Boston.[4]

The evidence strongly supports the conclusion that this organism is acquired postnatally. In our series of vaginal cultures it was not represented; further, Weinstein [18] in a large series, including infants with pathologic conditions, recovered Staph. aureus from the vaginas of only about 3 per cent. As shown in table 3, Staph. aureus is generally acquired by the newborn infant later than are the nonhemolytic streptococci; an abrupt rise in incidence occurs after the third day. In order of increasing importance the sources of implantation appear to be the fingers of adults, the air and oral droplets. The fingers of nurses frequently become contaminated with a hemolytic type of Staph. aureus during care of the infants. This occurred in 6 of 7 nurses from whose fingers cultures were obtained before, during or after contact, and in 10 of 16 hand impressions made by these 7 nurses (62.5 per cent); positive results in tests for coagulase were obtained with 96 per cent of the strains isolated. Even after scrubbing the hands and just prior to caring for another infant, 2 of 7 nurses still carried a coagulase-positive hemolytic strain of Staph. aureus on the fingers in four of sixteen tests (25 per cent). As has been suggested, the lower incidence and slower rate of implantation of the organism in infants in the ultraviolet wards treated with rays may have been due to almost complete elimination of the organisms from the air. In addition to a far greater total number of staphylococci in samples of air of the nonirradiated wards, over 80 per cent of the strains from these wards that were tested were coagulase positive, as compared with 42 per cent for the irradiated wards and 54 per cent for indoor, populated locations outside the hospital. However, the principal sources of infection were undoubtedly the noses and throats of adults. In detecting probable donors, strains from adults who had been in contact with the child were compared with the strain from the infant as regards type and degree of color, degree of hemolysis on rabbit blood agar plates, fermentation of mannitol and coagulase reaction. Particularly helpful was the color of growth on the crystal violet agar [20] of Chapman and Berens.[21] On this medium some strains of Staph. aureus produce a bright orange growth, others an orange with a violet rim and still others a violet growth. The color was sufficiently strain stable to be useful in matching. Another differential plating medium employed was the alkaline bromthymol blue lactose agar [20] of Chapman and his associates.[22] Most strains of Staph. aureus produce a yellow (acid) growth on this medium; a few, a gray-blue growth. Identity in all these characteristics between a strain isolated from an infant and one from an adult with whom there had been contact was required as evidence of identity and of probable source.

In table 9 the percentage distributions of pathogenic strains of Staph. aureus on the basis of the

19. Hallman, F. A.: Pathogenic Staphylococci in the Anterior Nares: Their Incidence and Differentiation, Proc. Soc. Exper. Biol. & Med. **36**:789 (June) 1937.

20. Obtained from Difco Laboratories, Detroit Mich.

21. Chapman, G. H., and Berens, C.: Crystal Violet Agar as a Differential Medium for Staphylococci, J. Bact. **29**:437 (May) 1935.

22. Chapman, G. H.; Lieb, C. W.; Berens, C., and Curcio, L.: The Isolation of Probable Pathogenic Staphylococci, J. Bact. **33**:533 (May) 1937.

color of the growth on crystal violet agar are reported. As may be seen, there is a close correspondence between the relative percentages of types occurring in the respiratory tracts of adults and of infants, 51 and 53 per cent violet colonies in cultures obtained from adults and from infants respectively, whereas only 8 per cent of the strains obtained from the fingers of adults were violet. The high percentage of violet strains in the air suggests the possibility of occasional primary implantation in the throats of infants from that source, but we believe that in the great majority of instances the transfer is direct from adult to infant through oral droplets.

TABLE 9.—*Distribution of Strains of Staphylococcus Aureus (Coagulase-Positive) as Differentiated on Crystal Violet Agar**

Source	Region	No. of Cases	No. of Strains	Percentages		
				Orange	Orange-Violet	Violet
Adult contacts	Nasopharynx and throat	40	48	17	32	51
Infants	Nasopharynx and throat	65	85	18	29	53
Nurses	Fingers	9	25	48	44	8
Air	Infant wards	..	65	37	3	60

* Chapman and Berens medium.

In table 10 the seasonal incidence of Staph. aureus in adult carriers and infants is outlined. The lowest rate of probable transfer was noted in September; the highest, in the period from January to June. The probable donors among the adult carriers were identified by successful matching with the strains which occurred in the infants. In each case the putative donor was the carrier who yielded the greatest number of staphylococci (Staph. aureus) from the throat and nasopharynx.

Colon Bacilli.—Of the 85 infants from whom nasopharyngeal cultures were obtained, 3.5 per cent showed the presence of some member of the colon group in the first day of life and 13.5 per cent within three days. The 31 strains which were classified were divided as follows: Esch. coli communis 75 per cent, Esch. coli communior 20 per cent and Aerobacter aerogenes 6 per cent. Forty per cent of the strains caused some degree of hemolysis on rabbit blood agar.

Our figures for the occurrence of bacteria of the colon group in the oral cavity were much lower than those reported by Gundel and Schwarz,[8] 40 per cent up to three days after birth, and, by Witkowski,[6] 48 per cent for the same site within two days. However, their infants were breast fed and 64 and 86 per cent respectively of the mothers had colon bacilli in the mouth. In our series the oral cavities of adults in contact with the infants was certainly not the source of implantations, as only 3 (4 per cent) of 70 of the adults from whom throat and nasal swabbings were cultured yielded Esch. coli. Although colon bacilli might be numerous in the air within incubators, they were rarely recovered from the air of the wards. The occurrence of members of the colon group in the nasopharyngeal flora of infants during the first week of life may conceivably be ascribed to implantation at the time of birth from the vaginal flora, but when these forms made their initial appearance at a later age they were probably received from other sources, principally by infant to infant transmission on the fingers of nurses and on various articles employed in their care. In 17 cultures from finger impressions of 4 nurses, Esch. coli was recovered in 10 instances during or after the care of an infant. One nurse, in 5 contacts with different infants, showed contamination of the fingers with Esch. coli on every occasion. Although tests revealed that in this instance washing the hands after each of these contacts removed the colon bacilli, it may well have been ineffective at other times. In fact, in one proved instance a nurse after thoroughly scrubbing her hands contaminated a nipple with colon bacilli in placing it on a feeding bottle.

Contrary to expectation, the evidence did not support the view that the primary implantation of the intestinal tract of newborn infants with Esch. coli was of oral origin. In investigating this point, specimens from the oral and rectal regions were cultured daily from the time of birth. The rectal specimens were taken on swabs and plated on Levine's eosin–methylene blue–lactose agar. In all 19 infants, the first rectal cultures which were positive for Esch. coli antedated the positive oral cultures. In 10, or 52 per cent, of these infants the rectal specimens were positive for Esch. coli within two days and in 16, or 84 per cent, within four days after birth, whereas this organism appeared in the nasopharynx at that age in less than 15 per cent of

TABLE 10.—*Seasonal Incidence of Hemolytic Strains of Staphylococcus Aureus in Adult Carriers and in Infants*

Period	Adults			Infants in Contact		
	Total	Carriers	Probable Donors	Total	Positive Cultures No.	Positive Cultures %
January-April.....	18	5	3	41	25	60
April-July.....	19	9	6	31	21	68
September.....	21	10	2	12	2	16.6
October-December.	20	7	3	18	8	44

a total of 85 infants. Of 4 of the infants whose rectal specimens contained members of the colon group within twenty-four hours after birth, 2 had Esch. coli communis and 2 A. aerogenes. In general, our results indicated that with the possible exception of Staph. aureus, the streptococci which are negative for fermentation of mannitol and the lactobacilli, initial bacterial seeding of the infant's colon is from sources other than swallowed bacteria.

Streptococci with proteolytic action on milk and gelatin were encountered with surprising frequency in the initial rectal floras (8 of 19 infants, or 42 per cent). In 7 of the 8 cases in which they were obtained these organisms were present within three days after birth. The strains produced no hemolysis on blood agar, but rather a green discoloration. Sherman, Stark and Mauer [23] recommended that this nonhemolytic, proteolytic streptococcus be designated as Streptococcus faecalis var. liquefaciens and that the name Streptococcus zymogenes be retained for the hemolytic but otherwise similar streptococci. This hemolytic type occurs in the intestinal flora of 6 to 10 per cent of adults, as determined by one of us.[24] Apparently, however, the alpha type of proteolytic streptococci is more often associated with pathologic conditions than is the hemolytic; all strains which Elser and Thomas [25] isolated from persons with pathologic conditions, including subacute endocarditis and appendicitis, belonged to the alpha variety.

COMMENT

The efficacy of the face mask as a protective device against direct transmission by droplets has been extensively studied in recent years. In some of these investigations pure cultures of distinctive strains of organisms such as Staph. aureus have been sprayed at the mask or test fabric covering a culture plate,[26] or a bacterial suspension in the air of an experimental chamber has been drawn by suction through the material to be tested and quantitative determinations of the filtering capacity made with the Wells's air centrifuge.[27] In other studies the mask under test was worn by persons who were carriers of mild pathogens [28] or whose mouths were enriched with Bacillus prodigiosus and its retentive capacity determined by having the subject speak, cough or sneeze toward a culture plate or air centrifuge.[29] Our observations are, we believe, the first in which the efficacy of the conventional mask used in hospitals was studied under wholly natural conditions. Under the conditions of observation, namely a 75 to 80 per cent sterility of the nasopharynx and throat of newborn infants and control of modes of transfer other than by oral droplets, the opportunity was provided to demonstrate the identity of the strain of streptococci initially implanted in an infant and of a strain from the upper respiratory passages of an adult with whom the child had been in contact. The masks employed were for the most part a four layer fine gauze (30 by 40 mesh) type, 4½ by 6½ inches (11.4 by 16.5 cm.) in size. In some instances a four layer butter-cloth mask was used. These masks are about midway between the most permeable and the least permeable in general usage in hospitals. Furthermore, it is pertinent to note that talking, except in rare instances, probably provided the sole force for propelling bacteria-laden droplets from the mouth through the fabric, as nurses and doctors who had colds were rigorously excluded from contact with the infants. Jennison,[30] through the medium of high speed photography with stroboscopic light, has shown that in ordinary conversation only a small number of demonstrable droplets are produced and that all but the most permeable face masks prevent their expulsion. It is possible, however, that the photographic method is inadequate to visualize the finest droplets capable of bearing bacteria. At any rate, our results provide proof that bacteria passed directly through the air from the adult to the infant in spite of the intervening face mask.

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30. Jennison, M. W.: Atomizing of Mouth and Nose Secretions into the Air as Revealed by High-Speed Photography, in Aerobiology, Publication 17, American Association for the Advancement of Science, 1942, p. 106.

There are numerous types of face masks, and some, experimental tests indicate, are effective protective devices and serve a useful purpose. McKhann, Steeger and Long [28b] in a recent article stated that according to various estimates the better types are 50 to 75 per cent effective. Unfortunately, those which are impermeable enough to hold back or deflect bacteria-laden droplets are generally uncomfortable to wear for extended periods, particularly in hot weather, and all tend to lose efficiency after long usage. Blatt and Dole [28b] reported that a six layer gauze mask remained effective for four hours, but at the end of twelve hours it had become useless, and if wet it lost its efficiency much sooner. The employment of face masks in the home in connection with the care of an infant is probably futile as a protective measure.

It cannot be claimed that the type of ultraviolet irradiation used in this study protects infants from direct transfer of pathogens by oral droplets during close contacts. On the other hand, it did seem to eliminate from the air of the wards practically all bacteria but the more resistant saprophytic types, and it is reasonable to suppose that air-borne infection from infant to infant through the medium of "droplet nuclei" or through infected dust was at least to some degree controlled. However, in the absence of epidemics [31] of infections of the respiratory tract in the wards during the period of study we had no opportunity to evaluate its effectiveness in that respect.

The results observed in cultures of material from the fingers impressed us with the difficulty of conducting entirely successful aseptic medical nursing in the care of infants in a hospital. Not only may occasional carelessness in washing hands permit the transfer of pathogens from infant to infant, but the surface of various articles, such as feeding bottles, trays and their contents, employed in the care of infants may become contaminated by handling by persons both in and outside the ward who are carriers of infection, and the infective agent in turn may be transferred to the infants on the fingers of persons in contact with them.

SUMMARY AND CONCLUSIONS

The initial aerobic bacterial flora of the throat and nasopharynx of artificially fed newborn infants is largely acquired through direct contact with adults and not from the parturient canal as claimed by Witkowski and others. The principal vehicle of transfer is droplets of saliva. The flora in premature infants is essentially the same as that reported by Kneeland for full term infants of similar age.

Although occasional contact with adult carriers of pathogens such as pneumococci, H. influenzae and beta hemolytic streptococci occurred, the first two organisms were not present and the hemolytic streptococci rarely present on the nasopharynx in 150 premature infants from 1 day to 4 weeks old. The observation that only one or two of the five or more fermentative types of nonhemolytic streptococci primarily implanted were able to persist suggests that the apparent absence of these pathogens may be due to failure of adjustment of the micro-organism to the immature mucous membrane rather than to the presence of specific immunologic factors.

Up to sixteen hours after birth the nasopharynges and throats of about 80 per cent of 16 infants exhibited sterility with the cultural methods employed. Between twenty-four and forty-eight hours after birth 50 per cent of 12 infants in wards exposed to ultraviolet irradiation still showed sterility, as contrasted with 12 per cent of 16 infants in wards not so exposed. Beyond that time results for the two groups were essentially alike except as regards hemolytic Staph. aureus.

Ultraviolet irradiation did not retard the acquisition of nonhemolytic streptococci but did delay infection with the hemolytic strains of Staph. aureus; in the absence of ultraviolet irradiation an occasional air-borne transfer of the latter organism probably occurred.

Our results indicated that ultraviolet irradiation, as applied, does not prevent person to person transmission of pathogens through the air within the range of a few feet. Among infants from 7 to 25 days old in wards without ultraviolet irradiation 60 per cent were carriers of hemolytic strains of Staph. aureus on the nasopharynx. Of 98 strains tested for the presence of coagulase 86 per cent gave positive results and thus presumably were potential pathogens.

The strains of streptococci and of Staph. aureus normally present in the throats and nasal passages of adults passed to some extent through the types of face masks worn, even in the absence of coughing and sneezing.

The acquisition of hemolytic strains of Staph. aureus was highest in the late winter and spring months and lowest in the early fall.

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31. Occasional infections occurred in all four rooms but were too few to provide a basis for conclusions regarding the effect of treatment of the air of a room. Aside from sporadic cases of nonspecific diarrhea, the infections were mainly due to a hemolytic strain of Staph. aureus. Three cutaneous infections, 1 attack of pneumonia and 1 of otitis media and 1 abscess of the buttock occurred.

KETOSIS IN RELATION TO THE HEPATIC RESERVES OF GLYCOGEN

A STUDY OF NORMAL * AND OF DIABETIC CHILDREN

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The susceptibility of children to the development of ketosis has been the subject of considerable study, especially with relation to the significance of ketone bodies in the production of acidosis and of cyclic vomiting. Since the publication of Gee's report in 1882 "On Fitful or Recurrent Vomiting," much has been written concerning the subject of cyclic vomiting, but it was not until 1903 that the importance of ketonemia in the syndrome was emphasized by Edsall.[1] There was relatively little clinical investigation in this connection until 1924, when Shaw and Moriarty [2] demonstrated that children have a greater tendency to have acidosis than do adults. They observed that during a fast of ten to fourteen days epileptic children rapidly acquired ketosis and acidosis. The level of the blood sugar dropped at the same time, reaching a minimum between the third and the eighth day of fasting. On subsequent days there was a tendency for the level of the blood sugar to rise, and toward the end of the fast the values were relatively normal. It was during the period of hypoglycemia that the most rapid development of acidosis occurred. This acidosis was ascribed to depletion of the stores of carbohydrate with an increased but incomplete combustion of fat, which in turn gave rise to ketone bodies. Similar observations have been made by other investigators.[3]

In accord with these observations, Ross and Josephs [4] were able to induce typical "attacks" in a child with cyclic vomiting by the sudden withdrawal of carbohydrate from the diet. During the attacks the child excreted ketone bodies, became drowsy, showed signs of acidosis and occasionally had convulsions. Heymann [5] precipitated similar attacks in susceptible children by means of ketogenic diets. The fact that ketosis develops at a lower fatty acid–dextrose ratio in normal children than in adults has been demonstrated by Wilson, Levine and Rivkin [6] and by Weymuller and Schloss.[7] The latter authors also presented evidence to indicate that the ability to store glycogen is the same in normal children as in those subject to cyclic vomiting.

On the basis of experimentation with animals, one of us [8] supported the hypothesis that since the metabolic rate of the infant or child is relatively higher than that of the adult, the extrahepatic tissues of the child utilize carbohydrate at a relatively greater rate than do those of the adult. If this is the case, a more rapid depletion of the hepatic reserves of glycogen should occur in the child, and any factor which tends to reduce the concentration of glycogen in the liver of the adult should produce a more rapid diminution in the child. This reduction would result in a greater susceptibility to ketosis, since it has been demonstrated that a decrease in the availability of glycogen from the liver is the principal stimulus for the oxidation of fatty acid and con-

* The term "normal" is employed to indicate average, healthy, nondiabetic children.

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sequently for the production of ketone bodies.[9] Hence, all of the conditions which are associated with ketosis in the child can be attributed to a relative depletion of glycogen from the liver with the sole exception of glycogenosis (von Gierke's disease), which can be explained by the fact that the glycogen in the liver is fixed and therefore is not available for utilization.

In spite of the apparent consensus that children are more susceptible than adults to the development of ketonemia and that carbohydrate impoverishment plays a role in this phenomenon, there are few quantitative data in reference to the hepatic reserves of glycogen of the child. It is now generally acknowledged that the liver is the only source of endogenous dextrose[10] and that the level of the blood sugar is dependent on the difference between the rate at which sugar is secreted into the blood by the liver and the rate at which it is removed from the circulation by the tissues. In the normal organism, in which the concentration of glycogen in the liver is relatively high, a sudden increase in the rate of removal of sugar from the blood stimulates the secretion of sugar by the liver and the amount of sugar in the blood remains essentially unchanged. However, when the store of glycogen in the liver is low a similar removal of sugar from the blood results in a decrease in the content of sugar in the blood, since the liver could not compensate adequately for the sudden excessive loss of sugar; as the store of glycogen becomes further impoverished the liver will draw on fat and protein for its energy, with the production of increased amounts of ketone bodies as one of the results.

These considerations led us to devise a procedure which can serve to gage the amount of glycogen stored in the liver in man.[11] When the renal threshold for sugar is lowered by means of intravenous administration of phlorhizin, an increased drain on the blood sugar and thereby on the reserves of glycogen in the liver is produced in accordance with the principles already outlined. Sugar removed from the blood via the kidneys (during the experimental period) can be measured in the urine excreted. As long as the level of the blood sugar remains unchanged, the excreted dextrose must be derived from glycogen from the reserves in the liver. However, when there is a decrease in the level of the blood sugar, the dextrose excreted in the urine represents not only that which has been secreted by the liver (from glycogen) but some free sugar which was originally present in the blood and other fluids of the body. By appropriate calculations the amount of sugar which must have originated in the liver can be estimated. Furthermore, if ketonemia occurs concomitantly with hypoglycemia, it is probable that the liver had only minimal reserves of glycogen and that the sugar which appears in the urine under these conditions takes origin from newly formed dextrose in the liver.

It is important to emphasize that the loss of sugar from the liver as measured by urinary excretion does not represent all of the glycogen which is released from the liver during the test. It represents only that extra amount of glycogen which is released to compensate for the loss of sugar from the blood in consequence of the decreased renal threshold and does not take into account the carbohydrate which is constantly being utilized. Therefore, the value designated as "loss from the liver" represents the actual reserve of glycogen in the liver at the beginning of the test, or the amount of glycogen over and above that required for utilization by the tissues. Recent studies by McCullagh and Lewis[12] in which the "phlorhizin test" was used in both human beings and animals confirm these conclusions.

It is apparent that if the liver of the child does not retain glycogen to the same degree as that of the adult the administration of phlorhizin, with the consequent glycosuria from the decrease in renal reabsorption of dextrose, will result in a lowering of the level of the blood sugar in a child, while in an adult the loss of the same amount of sugar will fail to change the level in the blood. The more severe the metabolic disturbance, the lower will be the reserve of glycogen and hence the greater the rapidity with which a decrease in the blood sugar will occur. For such reasons, the rapidity with which hypoglycemia and ketonemia develop in consequence of the removal of dextrose from the body via the kidneys provides a means of gaging the glycogen reserves of the liver of the normal or the diabetic organism.

METHOD

The details of the procedure employed were given in a previous publication.[11] All of the children tested,

9. Mirsky, I. A.: The Etiology of Diabetic Acidosis, J. A. M. A. **118**:690 (Feb. 28) 1942.

10. Mann, F. C.: The Role of the Liver as the Commissairiat of the Body, Am. J. Digest. Dis. & Nutrition **4**:355 (Aug.) 1937.

11. Mirsky, I. A.; Korenberg, M.; Nelson, N., and Nelson, W. E.: The Hepatic Glycogen Reserves in Diabetes Mellitus, Endocrinology **28**:358 (March) 1941.

12. (*a*) McCullagh, E. P., and Lewis, L. A.: Carbohydrate Metabolism of Patients Treated with Methyl Testosterone; Hypogonadism, J. Clin. Endocrinol. **2**: 507 (Aug.) 1942. (*b*) Lewis, L. A., and McCullagh, E. P.: Carbohydrate Metabolism of Animals Treated with Methyl Testosterone and Testosterone Propionate, ibid. **2**:502 (Aug.) 1942.

normal as well as diabetic, were permitted to have their regular evening meal on the day before the test. Some of the children received additional food at 9 p. m. in the form of orange juice and sucrose (cane sugar) in an amount sufficient to furnish 2 Gm. of carbohydrate per kilogram of body weight, and others received the additional carbohydrate at 3 a. m. Breakfast was omitted on the following morning and no food was permitted during the period of the test. The diabetic subjects did not receive their morning dose of insulin, and those who were receiving protamine zinc insulin were given regular insulin the day before the test.

The test was begun at 7:30 a. m. and completed six hours later. Water was allowed freely. A sample of blood was drawn at the beginning and again at the end of the six hours and was quantitatively analyzed for sugar by the Somogyi-Shaffer-Hartmann method [13] and for total ketone bodies by a modification of the Van Slyke and Fitz method.[14] Immediately after the withdrawal of the first sample of blood 1 Gm. of phlorhizin in solution was injected intravenously. The subject then emptied his bladder. Since the effect of the injected phlorhizin was lost fairly rapidly (complete inhibition of the reabsorption of dextrose lasting less than three hours), it was necessary to administer another gram of phlorhizin at the end of three hours in order to maintain a constant glycosuria. The urine was collected during the six hour interval, and the total amounts of dextrose and ketone bodies excreted were determined. At the end of the test the child was permitted to eat in order to compensate for the loss of sugar from the body.

The preparation of phlorhizin injected consisted of a solution of 1 Gm. of phlorhizin in 20 cc. of tenth-normal sodium hydroxide which had been boiled and permitted to return to the temperature of the body. Numerous tests revealed the solution of phlorhizin to be sterile. The solution was injected intravenously over a period of three to four minutes. In more than 200 persons thus treated, no damage to the veins occurred.

RESULTS

The present report is based on a study of 52 normal and 26 diabetic children. Of the normal group, 15 children received no pretreatment with extra carbohydrate, and 25 received extra carbohydrate at 9 p. m. and 12 at 3 a. m. The diabetic children were under good clinical control. Thirty-three tests were performed on diabetic subjects. Eleven children were given no extra carbohydrate; another 11, received extra carbohydrate at 9 p. m. and the remaining 11 at 3 a. m. The data obtained are summarized in figures 1 to 6.

The levels of blood sugar in normal children fell from 86 mg. to 67 mg. per hundred cubic centimeters, or 23 per cent, during the six hours of phlorhizination (fig. 1). The level of blood sugar in the children who received carbohydrate at 9 p. m. fell 9 mg. per hundred cubic centimeters, a decrease of 13 per cent, and in those who were fed at 3 a. m. the decrease was only 9 per cent. These data suggest that although an overnight fast results in a relatively rapid depletion of the glycogen of the liver the administration of extra carbohydrate during the night tends to lessen the drop in the level of the blood sugar.

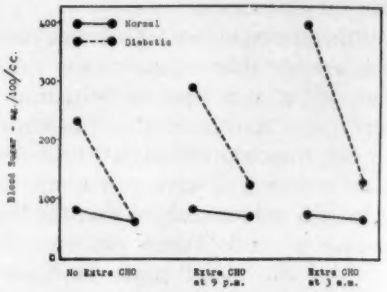

Fig. 1.—The influence of a six hour period of glycosuria produced by phlorhizin on the level of blood sugar in normal and in diabetic children. The effect of the administration of extra carbohydrate (CHO) at either 9 p. m. or 3 a. m. is illustrated.

The frequency of ketosis in consequence of the glycosuria due to the phlorhizination is indicative of the lability of the glycogen reserves (fig. 2). Thus 53 per cent of the normal children who were not given any extra carbohydrate had ketosis by the end of the test, while only 36 per cent of those fed at 9 p. m. and none of those fed at 3 a. m. acquired ketosis.

The diabetic children who were not given extra carbohydrate after their regular evening meal had a decrease of 172 mg. per hundred cubic centimeters, or 73 per cent, in their level of blood sugar (fig. 1); those fed additional carbohydrate at 9 p. m., a decrease of 164 mg. per hundred cubic centimeters, or 56 per cent, and those fed at 3 a. m., a decrease of 268 mg., or 67 per cent.

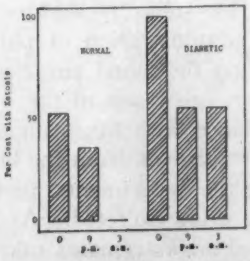

Fig. 2.—The incidence of ketosis in children consequent to a six hour period of glycosuria produced by phlorhizin. The decrease in the incidence of ketosis consequent to the administration of extra carbohydrate at either 9 p. m. or 3 a. m. is illustrated.

13. Somogyi, M.: Personal communication to the authors. Mirsky, Korenberg, Nelson and Nelson.[11]

14. Van Slyke, D. D., and Fitz, R.: The Determination of B-Hydroxybutyric and Acetoacetic Acid and Acetone Bodies in Blood, J. Biol. Chem. **32**:495 (Dec.) 1917.

It is obvious that the higher initial values for blood sugar in the latter groups are due to the extra carbohydrate. In figure 2 it will be noted that ketosis developed in all of the diabetic children who did not receive an extra feeding after their regular evening meal and in 55 per cent of

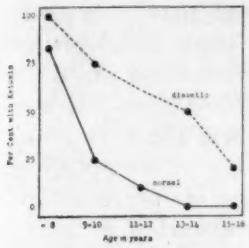

Fig. 3.—The relation of age of the child to the susceptibility to ketosis. The younger the child, the greater is the incidence of ketosis consequent to the glycosuria induced by phlorhizination.

those fed at 9 p. m. or at 3 a.m. Thus, it would appear that the extra feeding tended to decrease the incidence of ketosis consequent to the phlorhizination. It is of some interest that the administration of food at 3 a. m. was no more effective in preventing ketosis than the 9 p. m. feeding.

When the foregoing data are compared with those obtained for adults under similar circumstances,[11] a striking difference is noted. Normal adults had a decrease of only 3 per cent in the level of blood sugar after a phlorhizination period of six hours, whether or not they had been given extra carbohydrate. Furthermore, no normal adult acquired ketosis during the six hour period. On the other hand, an average decrease of 48 per cent in the level of blood sugar was observed in diabetic adults, in 50 per cent of whom ketosis developed during the same period of phlorhizination. Thus, the data in regard to ketosis in normal children are more like those for diabetic adults than those for normal adults.

In view of these observations, it seemed of interest to determine whether our data would reveal any age differences among children in regard to susceptibility to ketonemia (fig. 3). It is obvious that, within the age range of our group, the younger the children, the greater was the incidence of ketosis consequent to phlorhizination, whether diabetes was present or was not. It should be mentioned, however, that Heymann[15] noted that in infants in the first few months of life ketosis does not develop as readily as it does in children several years of age; there were no infants in our series.

The quantity of sugar lost which is derived from the glycogen of the liver provides an additional means of comparison of the different groups. In brief, it is estimated by subtracting from the total sugar excreted in the urine that which comes directly from the blood and is reflected by the drop in blood sugar.[11] The data can be expressed in two ways: as "total loss of dextrose from glycogen of the liver" (fig. 4) or as "loss of dextrose from glycogen from the liver per kilogram of body weight" (fig. 5). Thus, the average total loss for normal adults who received no extra carbohydrate was 19 Gm. of dextrose (from glycogen), or 289 mg. per kilogram of body weight. The average loss for normal children who received no extra carbohydrate was 16.3 Gm. in total, or 390 mg. of dextrose of hepatic origin per kilogram of body weight. The average total loss from the livers of normal children receiving extra carbohydrate at 9 p. m. and 3 a. m. was 15.7 Gm. and 15.0 Gm. respectively. When the data are expressed as loss of dextrose derived from glycogen of the liver per kilogram of body weight, it will be observed that children

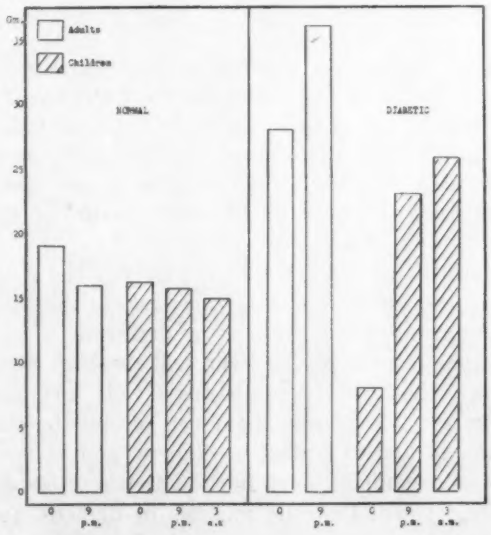

Fig. 4.—The total loss of dextrose derived from hepatic glycogen during and after a six hour period of glycosuria, computed from the total sugar excreted in the urine minus the amount due to the fall in blood sugar. The effect of the administration of extra carbohydrate at 9 p. m. or at 3 a. m. is illustrated.

have a proportionately greater breakdown of hepatic glycogen than do adults during the same experimental period (fig. 5).

The administration of extra sugar to the children with diabetes made more glycogen available for storage. Thus, while diabetic children who

15. Heymann, W.: Metabolism Studies on Age Disposition to Ketosis in Human Beings, J. Pediat. **12**:21 (Jan.) 1938.

received no extra carbohydrate lost an average of only 8.1 Gm. of dextrose, those who received extra carbohydrate at 9 p. m. and 3 a. m. lost 22.9 and 25.8 Gm. respectively (fig. 4). This increased excretion of sugar can be attributed only to the extra carbohydrate fed the children.

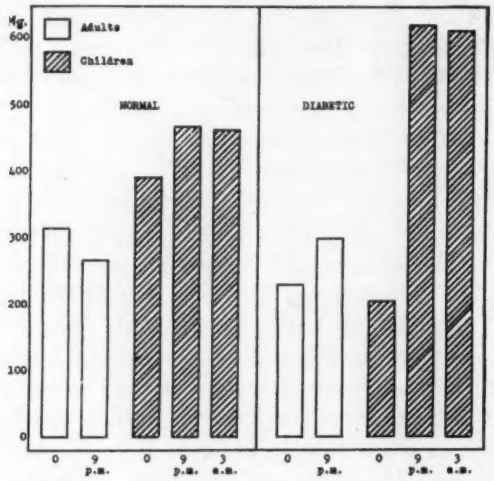

Fig. 5.—The loss of dextrose derived from hepatic glycogen per kilogram of body weight during and after a six hour period of glycosuria. The effect of the administration of extra carbohydrate at 9 p. m. or at 3 a. m. is illustrated.

COMMENT

There are now considerable data in support of the hypothesis that a diminution in the amount of available glycogen in the liver is the essential prerequisite for an increase in the oxidation of fatty acids which in turn results in an accelerated rate of formation of ketone bodies in the liver and a consequent ketonemia.[9] Thus, it has been demonstrated that the liver is the main site of the formation of ketone bodies; that any phenomenon which induces a depletion of the glycogen reserve in the liver will produce ketonemia; that the administration of adequate amounts of exogenous sugar can inhibit the formation of ketone bodies in diabetic and in nondiabetic organisms, even in the absence of insulin in the former; that the muscles of diabetic and of normal animals utilize ketone bodies with equal avidity; that there is a maximal rate at which ketone bodies are utilized by the muscles, and that excessive ketonemia will occur only when the rate of production exceeds that of utilization; that carbohydrate metabolism does not affect the rate at which ketone bodies are burned in the muscles, and that so long as the organism can maintain an adequate store or reserve of glycogen in the liver the rate of fat metabolism, and therefore the rate of formation of ketone bodies, cannot become sufficiently increased to cause an excessive ketonemia. Accordingly, it may now be stated that fats do not "burn in the flames of carbohydrate" but "the flames of carbohydrate inhibit those of fat."

The rapidity with which the liver can be depleted of glycogen is dependent in a large measure on the amount present in that organ. Since ketogenesis is stimulated by a depletion of glycogen in the liver, it is apparent that the amount of this store or reserve of glycogen is a significant determinant in the susceptibility of the organism to ketosis. It has been known for some time that the liver of a person with diabetes has a low reserve of glycogen because the relative rates of formation and breakdown of glycogen are disturbed in favor of the latter. Hence, it is not surprising to note that the removal of relatively small amounts of glycogen (fig. 6) from the liver of the diabetic adult or child so intensifies the metabolic disturbance that there results a decreased ability to maintain the level of the blood sugar and an increased incidence of ketosis.

Comparison of data obtained for normal children and for adults[11] reveals that during a six hour period of glycosuria induced by intravenous administration of phlorhizin (fig. 6) normal children show a greater degree of hypoglycemia and a greater incidence of ketosis associated with

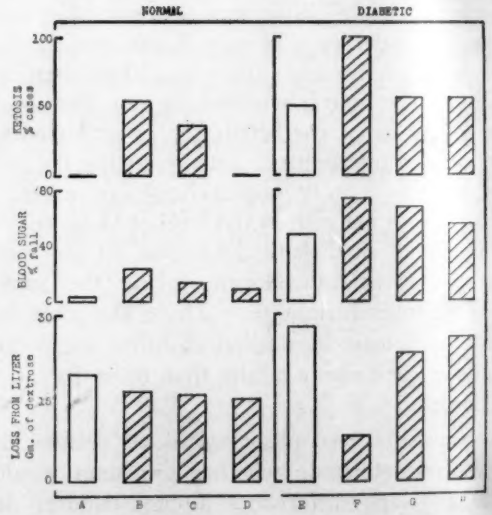

Fig. 6.—The influence of loss of glycogen from the liver on the blood sugar level and on the incidence of ketosis. The cross-hatched boxes refer to children; the blank boxes, to adults. A, B, E and F received no extra carbohydrate. C and G received 2 Gm. per kilogram at 9 p. m. and D and H at 3 a. m.

a relatively smaller loss of sugar of hepatic origin, when computed on the basis of the whole body weight. This indicates that the loss from the liver of an amount of glycogen which produces no effect in the normal adult (fig. 6, *A*) is ade-

quate to deplete the hepatic reserves of glycogen of the child (fig. 6, *B*).

From the preceding analysis it may be observed that the normal child (fig. 6 *B*) behaves somewhat like the diabetic adult (fig. 6 *E*) in relation to the development of ketosis consequent to loss of glycogen from the liver. Hence, it may be inferred that the normal child, like the diabetic adult, has a low reserve of glycogen in the liver, so that an extra loss of from 15 to 20 Gm. of dextrose in six hours is adequate to deplete this store. Furthermore, it is apparent that the diabetic child (fig. 6 *F*) differs from the normal child (fig. 6 *B*) in that a smaller loss of sugar from hepatic glycogen results in a greater fall in the blood sugar level and a greater incidence of ketosis; stated in another way, the hepatic reserves of glycogen are smaller in the diabetic child.

In support of this deduction is the observation that when extra carbohydrate is given at various intervals before the phlorhizination a loss of from 15 to 20 Gm. of dextrose from the hepatic reserve of glycogen does not produce as great a drop in the blood sugar level and the incidence of ketosis is decreased (fig. 6). It is inferred that the extra carbohydrate administered late at night increased the hepatic reserves of glycogen so that when a new demand for sugar was made more adequate stores were available. This is true for the diabetic child as well as for the normal child, since the extra carbohydrate not only made possible a greater amount of hepatic glycogen for subsequent secretion (fig. 6, *G* and *H*) but resulted in a decrease in the incidence of ketosis.

It is apparent that a more precise measurement of hepatic reserves of glycogen would be the determination of the amount of carbohydrate (of hepatic origin) excreted from the onset of the test to the time at which ketosis first occurs. This was done for 10 normal children ranging in age from 8 to 12 years, and it was calculated that an amount of glycogen approximately equivalent to 15 Gm. of dextrose was present in the liver above the amount ordinarily used for oxidative purposes. The period of six hours utilized in the present study usually was adequate to deplete the glycogen reserves of normal children.

In accordance with the data presented it can be anticipated that any phenomenon which will increase the metabolic demand of the muscles for carbohydrate (e. g. high body temperature) or which will decrease the availability of carbohydrate for storage in the liver (e. g. vomiting) will favor the development of ketonemia. Hypoglycemia in such situations will occur only until the rate of formation of sugar from noncarbohydrate sources catches up with the rate at which the liver is losing its glycogen. This is in agreement with the earlier observations that a fast for a short period will produce hypoglycemia in children within a few days, after which the blood sugar returns to normal. The same period of fasting does not have such an effect in the adult. Thus it must be emphasized that in the presence of any infection or metabolic disturbance in the child a constant and adequate supply of exogenous carbohydrate should be made available. The administration of frequent meals, if necessary at night as well as during the day, should eliminate the increased susceptibility to ketosis which sick children exhibit and consequently prevent the deleterious effects of ketosis and its contribution to the development of acidosis.

SUMMARY

Administration of phlorhizin and the consequent glycosuria result in removal of sugar from the blood, which in turn induces a compensatory increase in the breakdown of glycogen in the liver. When the hepatic reserves of glycogen are adequate, the blood sugar remains relatively constant during and after a short period of phlorhizination. When the hepatic reserves of glycogen are inadequate hypoglycemia and ketonemia develop as soon as a relatively small amount of sugar is lost from the body.

Removal by glycosuria of from 15 to 20 Gm. of sugar from the normal child or of a lesser amount from the diabetic child results in an impoverishment of the liver with respect to glycogen and consequent development of hypoglycemia and ketonemia. Loss of 15 to 20 Gm. of sugar by the normal adult does not produce such an effect, but in the diabetic adult it results in a decrease in the blood sugar and the development of ketonemia.

The younger the child, the smaller is the relative reserve of glycogen in the liver, which accounts for the inverse correlation between the age of the child and the incidence of ketonemia.

The administration of extra carbohydrate results in a greater storage of glycogen in the liver and thereby decreases the susceptibility to ketosis. In the presence of infections or other metabolic disturbances in the child frequent feedings of carbohydrate should be provided.

Jewish Hospital.
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ELECTROCARDIOGRAPHIC VARIATIONS IN ACUTE GLOMERULONEPHRITIS

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PHILADELPHIA

The earliest known report of dilatation of the heart in acute glomerulonephritis was published by Goodhart[1] in 1879. Since the appearance of these original observations, interest in the cardiac manifestations of acute glomerulonephritis has followed a somewhat cyclic course with a sudden upward acceleration in recent years. Clinicians in various parts of the world, impressed anew with the prominence of circulatory symptoms in many patients with this disease, have been stimulated to make careful studies of the cardiac condition. As one result of this intensification of interest, observations on serial electrocardiograms taken from patients ill with acute glomerulonephritis have been published[2] (table 5). Only one such study has dealt solely with children.[2f] In an earlier analysis of tracings taken from adults and children, it was reported that the electrocardiographic changes in patients 15 years or less were not so marked as in adults.[2e] The present paper presents a report of the variations noted in electrocardiograms obtained from patients in the Children's Hospital in Philadelphia, where for over ten years detailed observations have been made on all children admitted with a diagnosis of nephritis.[3]

For the purpose of this analysis of electrocardiographic variations, the records of the first 50 children from whom at least two electrocardiograms had been taken during a first attack of acute glomerulonephritis were chosen. No attempt was made to pick out patients presenting predominant cardiac symptoms; the number of tracings taken and the absence of any preceding history of nephritis were the sole criteria for selection. The average number of tracings made for each patient was five and nine-tenths, with limits ranging from two to seventeen. Precordial leads were not used.

The ages ranged from 4 months to 13 years, the average being 6.3 years. Forty-four children, or 88 per cent, were below the age of 10 years; 20, or 40 per cent, below the age of 6 years. There were 30 boys and 20 girls. Recovery occurred in all instances.

A history of an infection shortly preceding the onset of nephritis was obtained for all but 3 children. In 70 per cent this preceding infection involved the upper respiratory tract and contiguous structures. Many children still presented signs of inflammation of the upper respiratory tract, pharynx and ears at the time of admission to the hospital. Scarlet fever had preceded onset in 14 per cent.

In all cases at least one electrocardiogram had been obtained during the first month following the appearance of hematuria or edema, the initial tracings for 30 patients having been taken during the first week following onset and for 11 patients during the second week.

INFLUENCE OF DRUGS

Since only 9 patients had received no medication it seemed advisable to determine the possible influence of digitalis, magnesium sulfate and sulfanilamide (drugs which had at times been administered in large doses) before evaluating changes which might have been due to nephritis.

From the Department of Pediatrics, School of Medicine, University of Pennsylvania, and the Children's Hospital.

1. Goodhart, J. F.: On Acute Dilatation of the Heart as a Cause of Death in Scarlatinal Dropsy, Guy's Hosp. Rep. **24**:154, 1879.

2. (*a*) Tur, A.: Electrocardiographic Studies in Acute Diffuse Glomerulonephritis, Klin. med. **13**:1372, 1935. (*b*) Master, A. M., and Dack, S.: Electrocardiogram in Acute Nephritis, abstracted, Am. Heart J. **12**:244, 1936. (*c*) Master, A. M.; Jaffe, H. L., and Dack, S.: The Heart in Acute Nephritis, Arch. Int. Med. **60**:1016 (Dec.) 1937. (*d*) Langendorf, R., and Pick, A.: Elektrokardiogramm bei akuter Nephritis, Med. Klin. **33**:126, 1937; Acta med. Scandinav. **94**:1, 1938. (*e*) Garreton Silva, A.; Hervé, L.; Noguès, F., and Forero, L. G.: Les troubles de l'électrocardiogramme au cours de la néphrite aiguë, Arch. d. mal. du cœur **31**:217, 1938. (*f*) Cossio, P.; Arana, R., and Kreutzer, R.: Alteraciones del electrocardiograma en la glomerulonefritis difusa aguda, Rev. argent. de cardiol. **6**:283, 1939. (*g*) Williams, R. D.: Electrocardiographic Changes in Acute Hemorrhagic Nephritis, Bull. Johns Hopkins Hosp. **65**:434, 1939.

3. Rubin, M. I., and Rapoport, M.: The Three Major Complications of Acute Hemorrhagic Nephritis in Children: Their Prevention and Treatment, Pennsylvania M. J. **40**:1029, 1937; Cardiac Complications of Acute Hemorrhagic Nephritis, Am. J. Dis. Child. **55**:244 (Feb.) 1938; The Mode of Action of Magnesium Sulphate in Reducing the Hypertension of Acute Glomerulonephritis, Am. J. M. Sc. **201**:734, 1941. Rubin, M. I.; Rapoport, M., and Waltz, A. D.: A Comparison of Routine Urinalysis, Addis Count and Blood Sedimentation Rate as Criteria of Activity in Acute Glomerulonephritis, J. Pediat. **20**:32, 1942.

Digitalis.—The characteristic electrocardiographic changes due to the administration of digitalis are too well known to warrant description in this paper. Twelve patients had received digitalis. Transient prolongation of the PR interval was noted in 3; shift of the pacemaker from the sinus to the auriculoventricular node in 2 and low P waves in 1. Slight depression of the ST segment in leads I and II was noted 7 times, with the segment remaining horizontal or being curved upward. This is not typical of digitalis intoxication in which sagging is usually associated with a downward inclination of the ST segment. Similar changes in the ST segment were present, moreover, in the tracings of 7 patients who had received no digitalis. Although inversion of T waves occurred four times in lead I, once in lead III and once in all three leads at a time when digitalis was being administered, the type of inversion did not resemble that due to this drug. Inversion of T waves in the electrocardiograms of these children with acute nephritis was invariably late, preceded by an ST segment which curved upward or remained horizontal. Similar inverted or diphasic T waves were noted in the tracings of 15 patients who had received no digitalis.

The high tolerance to digitalis was in fact striking. Doses ranging from 1 to 3 grains (0.06 to 0.18 Gm.) of digitalis U. S. P. X per 10 pounds (4.5 Kg.) body weight after loss of edema were given rapidly, often within a period of only twelve to eighteen hours, with no electrocardiographic signs of toxicity more severe than a brief prolongation of the PR interval. This tolerance was in sharp contrast to the reaction in patients with acute rheumatic infection in whom much smaller doses have not infrequently produced definite electrocardiographic signs of the effects of digitalis.

Sulfanilamide.—The administration of sulfanilamide has been stated to result in a slight lowering of the amplitude of T waves and slight depression of the ST segment.[4] No waning of T waves was noted in 8 of 24 patients who had received sulfanilamide. In 3 children the appearance of low T waves failed to coincide with the time of administration of the drug. Edema must be considered as a possible cause for decreased amplitude of T waves in 5 patients, particularly since all leads were involved and the amplitude of the R waves was lowered at the same time.

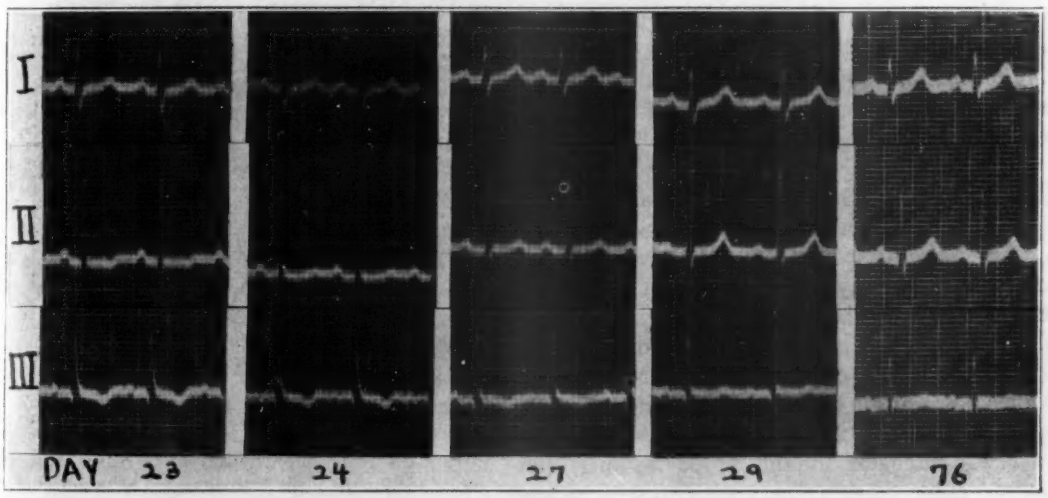

Fig. 1.—Electrocardiograms of a boy aged 7 years. The heart was normal clinically; there was no edema; the maximum blood pressure was 130 systolic, 70 diastolic. The patient received sulfanilamide from the twenty-second to the twenty-sixth day inclusive, but no digitalis.

Lowered amplitude of T wave in lead I, twenty-third day; diphasic T wave in lead II, twenty-third and twenty-fourth days; low T wave in lead II, twenty-seventh day; inverted T wave in lead III, twenty-third to twenty-seventh day, with slight upward bowing of ST segment; depressed ST in leads I and II, twenty-third and twenty-fourth days.

Finally, in 8 patients with no clinically apparent edema, waning of T waves which occurred at the time of administration of sulfanilamide may have been produced by the drug. The ingestion of sulfanilamide may also have been a contributing factor in the lowering of the ST segment in the electrocardiograms of 7 patients (fig. 1). It is to be remembered, however, that medication with sulfanilamide, usually begun promptly after admission, coincided with the period in which clinical symptoms and signs were most evident. Similar slight sagging of the ST segment occurred in the tracings of 7 patients who had received no sulfanilamide.

4. Katz, L.: Personal communication to the authors.

Magnesium Sulfate.—Miller and Van Dellen [5] reported that electrocardiograms of dogs taken after the intravenous injection of 10 cc. of a 20 per cent solution of magnesium sulfate showed an early acceleration of rate followed by slowing, prolongation of the PR and QS intervals and increased excursion of all complexes. Tracings reproduced in their paper show high, peaked T and P waves. Bernstein and Simkins [6] noted that after the intravenous injection of 10 cc. of 10 per cent magnesium sulfate solution into adult human beings there occurred slight changes in the QRS complex or in the T wave; in general, there were as many changes in one direction as in the other. Hirschfelder and Haury [7] stated that in normal animals and in normal human beings the plasma magnesium is scarcely raised by ordinary doses of ingested magnesium sulfate. In patients with renal disease, however, rapid and intense increase in plasma magnesium follows ingestion of magnesium sulfate.

In the Children's Hospital at the present time magnesium sulfate is used for the treatment of hypertension in acute glomerulonephritis in doses of 0.2 cc. of 50 per cent solution per kilogram of body weight, given intramuscularly and repeated when necessary at intervals of four hours or more. It was given for periods ranging from one to five days to 25 of the 50 patients in the group described in this paper. It is conceivable that a rise of plasma magnesium may have occurred in some of the patients treated with magnesium. In all but 4 of these patients some degree of nitrogen retention was present (average urea nitrogen in the blood 32 mg. per hundred cubic centimeters, with limits of 18 and 67), presumably due to diminished urinary output resulting from blocking of the glomeruli.

High, peaked T waves (fig. 5) were present in the electrocardiograms of 3 of the 25 patients who had received magnesium sulfate, but not at a time synchronous with the administration of the drug. Intervals varying from three to fifteen days had elapsed between cessation of ingestion of the drug and the appearance of the high, peaked T waves. Similar waves, moreover, were noted in the tracings of one person who had never received magnesium. Transient increase in amplitude of T waves, of moderate degree, was detected in the tracings of 5 additional patients who had received magnesium sulfate and of 7 to whom the drug had not been given. It would not seem possible, therefore, to ascribe the increased excursion of T waves to the administration of magnesium. Decreased amplitude of T waves was observed in the electrocardiograms of 12 patients, associated in all cases with low R waves. Digitalis had been administered to 7 children and sulfanilamide to 3 while they were still receiving magnesium. Edema, cardiac failure or the ingestion of sulfanilamide is a more probable cause than is the administration of magnesium for the lowering of T waves in these children. The single instance of prolongation of the QRS interval in this series occurred in a child who had received no magnesium sulfate.

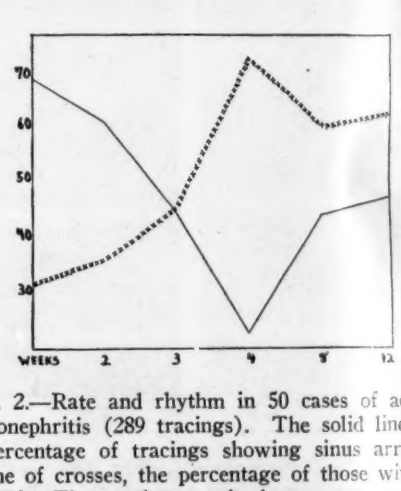

Fig. 2.—Rate and rhythm in 50 cases of acute glomerulonephritis (289 tracings). The solid line denotes the percentage of tracings showing sinus arrhythmia; the line of crosses, the percentage of those with a rate above 90. The numbers at the bottom represent weeks from the time of onset of nephritis.

ANALYSIS OF ELECTROCARDIOGRAMS

Rate and Rhythm (fig. 2).—In over 60 per cent of the tracings taken within the first two weeks after the onset of glomerulonephritis, sinus arrhythmia, frequently of considerable degree, was present and the cardiac rate was 90 or below. In 8 initial tracings taken within the first two weeks of illness, the cardiac rate was below 75; in only 5 was it over 120. A tendency toward acceleration of rate became noticeable toward the end of the third week. During the fourth week, the rate recorded in over 70 per cent of the tracings was above 100. At the same time the rhythm had become regular in almost 80 per cent. In the subsequent two months there was a gradual rise in the incidence of sinus arrhythmia together with a slight reduction in the number of tracings with rapid rate.

5. Miller, J. R., and Van Dellen, T. R.: Electrocardiographic Changes Following Intravenous Administration of Magnesium Sulphate, J. Lab. & Clin. Med. **23**:914, 1938.

6. Bernstein, M., and Simkins, S.: Magnesium: The Effects of Intravenous Injections on the Human Heart, J. Lab. & Clin. Med. **25**:131, 1939.

7. Hirschfelder, A. D., and Haury, V. G.: Clinical Manifestations of High and Low Plasma Magnesium: Dangers of Epsom Salt Purgation in Nephritis, J. A. M. A. **102**:1138 (April 7) 1934; Effect of Renal Insufficiency upon Plasma Magnesium and Magnesium Excretion After Ingestion of Magnesium Sulphate, J. Biol. Chem. **104**:647, 1934.

That the general tendency toward sinus arrhythmia and bradycardia shortly after the onset of clinical symptoms of glomerulonephritis is related to the existence of hypertension and stimulation of the vagus would seem obvious. With few exceptions these children were hypertensive at the time of admission to the hospital, the average systolic pressure being 142 (limits 238 and 100) and the average diastolic pressure 107 (limits 170 and 70). By the fourth week, when regular rhythm and tachycardia predominated, the blood pressure as a rule had returned to normal.

Volhard[8] placed great significance on the presence of tachycardia as a sign of cardiac failure in a febrile adult with acute glomerulonephritis. A slow pulse, in his opinion, was a good prognostic sign; even a normal pulse rate of 80 was undesirable and a signal that the heart should be watched, whereas a rate of 100 or above was a definite indication of danger. No relation between tachycardia and heart failure was noted in the present group of children. The tendency for tachycardia to develop in the third and fourth weeks after the onset of illness would seem to be a physiologic phenomenon related to the drop in blood pressure. Of the 22 children who showed a cardiac rate of 90 or above in tracings taken during the first two weeks of the disease, 12 had relatively low maximum blood pressures (average 109 systolic, 76 diastolic). Only 1 child in this group showed any signs of cardiac failure—a boy of 5 years in whom enlargement of the heart and the liver developed following a mastoidectomy performed on the fifteenth day of his nephritis. In the remaining 10 children the maximum blood pressure was high (average 153 systolic, 113 diastolic). In 7 of these children heart failure developed. Five of the 7 were febrile throughout the time of rapid pulse; in the other 2 the cardiac rate remained above 100 through the period of convalescence and recovery.

Transient premature auricular contractions were noted in 1 patient and persistent premature ventricular contractions (still present two and a half years following onset) in another. There were 2 instances of sinus arrest, each appearing in the first tracing of a series.

Changes in the P Wave (table 1).—Transient changes in the P wave, not related to the administration of digitalis were noted 18 times. In only 1 case was there a definite correlation between the appearance of high P waves and cardiac failure (fig. 3). In 14 children, changes in the P wave seemed to bear a direct relation to the existence of sinus arrhythmia and bradycardia (low P or shifting pacemaker) or of tachycardia (high P).

Disturbances in Conduction.—The only 2 instances of duration of the PR interval beyond the normal for age and rate[9] not related to administration of digitalis were persistent but of only slight degree (0.16 second in a child of 3 years; 0.20 second in a child of 11 years). One instance of transient slight prolongation of QRS was noted, and there were 2 cases of sinus arrest.

Abnormalities in the QRS Complex.—Low voltage, producing a highest excursion of less than 5 mm., was noted only 3 times. Decreased amplitude of R waves in tracings taken early in the course of the illness, however, was present 30 times (figs. 4 and 8). As was to be expected, this decrease in voltage to a certain extent could be correlated with the presence of edema at the time of admission to the hospital. These 30 children were all edematous, the gain in weight due to edema fluid varying from 4 to 26 per cent and averaging 11 per cent of their minimal weight. Among the group showing no change in amplitude of R waves, no edema could be detected in 3 of the patients, and in the remainder the loss in weight due to disappearance of edema averaged only 5.3 per cent, with limits of 0.2 and 19 per cent. Correlation between height of R wave and the presence or extent of edema was by no means absolute, however. A few patients with mild edema had greater decreases in voltage than others who were more edematous. In 5 children with increases of more than 10 per cent in weight due to edema, there was no noticeable lowering in the amplitude of the R waves.

It was interesting in several cases to observe the rise in height of R waves with the disappearance of edema and the subsequent lowering as the children improved in nutrition and finally became obese.

TABLE 1.—*Transient Variations in the P Wave in 50 Cases of Acute Glomerulonephritis*

	Shifting Pacemaker	High	Low	Notched
Transient	8	5	7	1
Related to:				
Digitalis	2	..	1	..
Heart failure	..	1	..	1
Sinus arrhythmia and bradycardia	6	..	5	..
Tachycardia	..	3	..	..
No relation to rate, drugs or heart failure	..	1	1	..

8. Volhard, F.: Handbuch der inneren Medezin, Berlin, Julius Springer, 1931, vol. 6, pt. 2, pp. 1278-1282.

9. Ashman, R., and Hull, E.: Essentials of Electrocardiography for the Student and Practitioner of Medicine, ed. 1, New York, The Macmillan Company, 1937, table 1, p. 204.

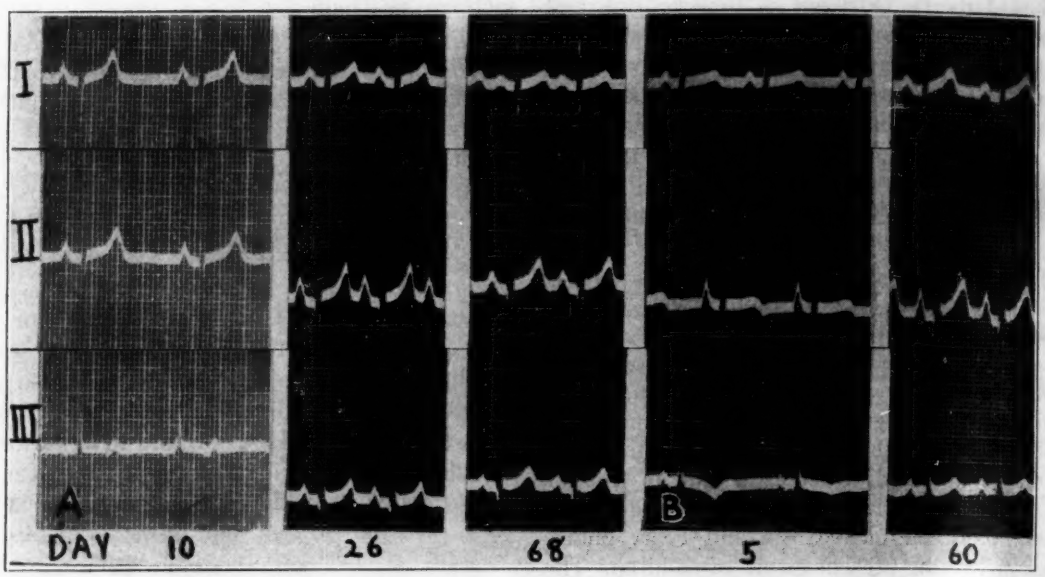

Fig. 3.—Electrocardiograms of a girl aged 2 years. The heart and liver were enlarged; there had been 18 per cent increase in weight due to edema; the maximum blood pressure was 160 systolic, 110 diastolic. *A* is a tracing made during the first attack of acute glomerulonephritis. Venous pressure on the thirteenth day was 28 cm. of water. The patient received magnesium sulfate on the tenth and eleventh days, sulfanilamide for seventy days and digitalis on the twelfth day (1.6 grains per 10 pounds [4.5 Kg.] of body weight). *B* shows tracings made during recurrence of glomerulonephritis one year later. The heart and liver were enlarged. No digitalis was administered.

A, diphasic T wave in lead III on the tenth day; slight deviation of the axis to the right and high P in lead II the twenty-sixth day. *B*, deviation of the axis to the right, low T wave in lead I; diphasic T in lead II and inverted T in lead III on the fifth day; high P in lead II on the fifth and sixtieth days.

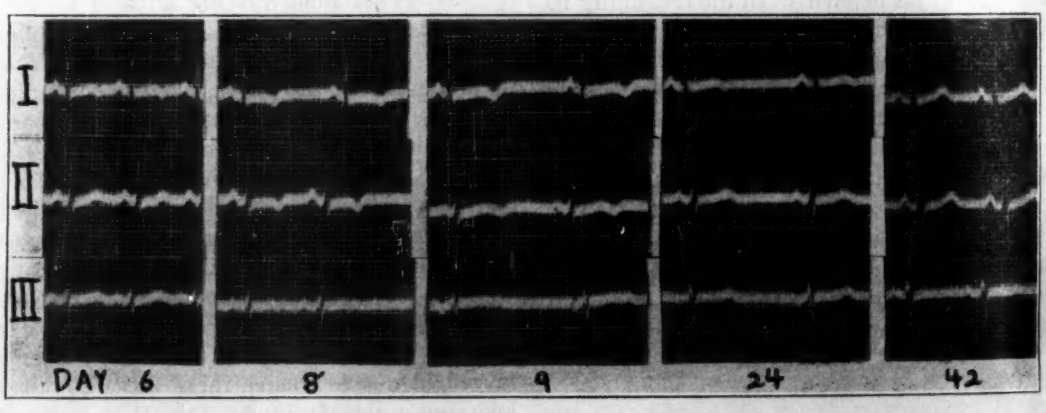

Fig. 4.—Electrocardiograms of a boy aged 9 years, with tachycardia, systolic gallop, a large, tender liver, a 20 per cent increase in weight due to edema and a maximum blood pressure of 150 systolic, 120 diastolic. The patient received magnesium sulfate on the seventh day and digitalis on the eighth and ninth days (2 grains per 10 pounds of body weight).

Decreased amplitude of QRS in early tracings; late inversion of the T wave in lead I from the sixth to the twenty-fourth day; late inversion of the T wave in lead II on the eighth and ninth days, in both instances preceded by upward bowing of the ST segment; diphasic T wave in lead III on the eighth and ninth days; depression of ST in leads I and II on the sixth to the ninth day.

Slurred R waves were observed as a transient phenomenon 3 times and were persistent in 2 cases.

A transient increase in the depth of S or Q waves occurred in 7 children (figs. 3, 5 and 8), all but 2 of whom evidenced signs of cardiac failure with associated enlargement of the liver.

Slight deviation of the electrical axis to the left (negative QRS complex in lead III) was noted 10 times; in 3 cases it was persistent. If one may judge from the configuration of the T wave in leads I and III,[10] change in position of the heart due to elevation of the diaphragm may have been a contributing factor in 2 children in whose tracing the T wave in lead I was high and in lead III inverted during the period of transient shift of the axis to the left (fig. 5). In 4 children the amplitude of the T wave in lead I was decreased (to the point of inversion in 2) and that in lead III increased during the period of deviation to the left. All 4 of these children and 1 child in the preceding group presented clinical signs of heart failure. Transient deviation of the electrical axis to the right, as evidenced by increased depth of the S wave in lead I (fig. 3) was noted in the electrocardiograms of 2 children, both of whom showed associated

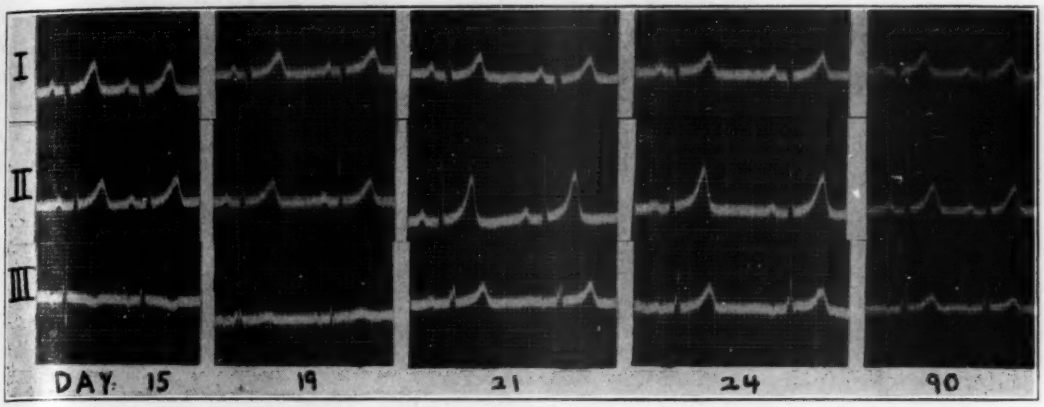

Fig. 5.—Electrocardiograms of a boy aged 7 years, with his heart normal clinically, an 8 per cent increase in weight due to edema and a maximum blood pressure of 164 systolic, 138 diastolic. The patient received magnesium sulfate on the thirteenth, sixteenth and eighteenth days.

Transient left axis deviation on the fifteenth day with inversion of the T wave in lead III. High, peaked T waves in lead II on the twenty-first and twenty-fourth days.

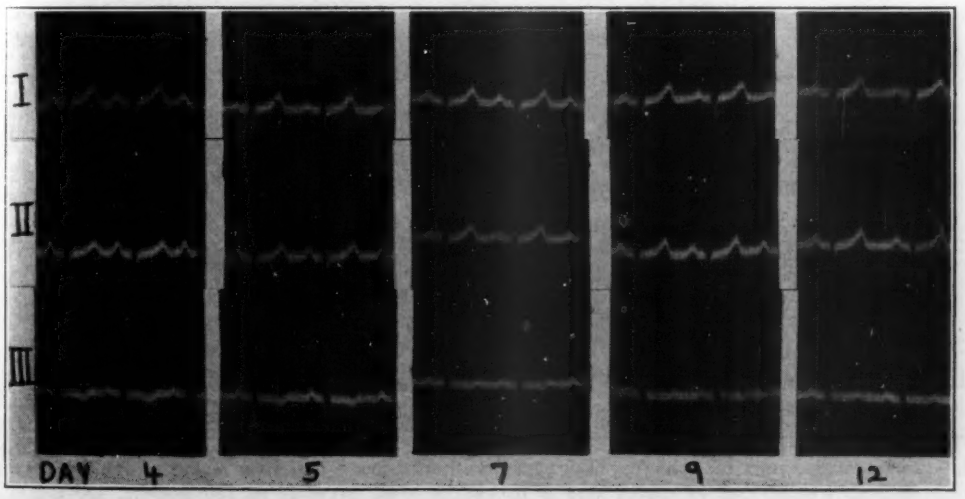

Fig. 6.—Electrocardiograms of a boy aged 4 years, with his heart normal clinically, a 5 per cent increase in weight due to edema and a maximum blood pressure of 110 systolic, 84 diastolic. No drugs were administered.

Late inversion of the T wave in lead III on the fourth and fifth days, with slight upward bowing of the ST segment. Depressed ST in lead III on the fourth and fifth days.

10. Proger, S. H., and Minnich, W. R.: Left Axis Deviation With and Without Heart Disease, Am. J. M. Sc. **189**:674, 1935.

cardiac failure and enlargement of the liver. In addition, there were 4 patients whose early tracings showed a lower R wave in lead I and higher R wave in lead III than did their later tracings.

Changes in the T Wave (table 2).—Although lowered amplitude of T waves in one or more leads was noted in the electrocardiograms of 31 patients, in all but 13 of these the presence of patients, 10 times in lead I, twice in lead II and 13 times in lead III (in 2 of the 13 instances in association with deviation of the axis to the left). Late inversion was the rule, the preceding ST segment being horizontal or curved upward, with occasional slight sagging. Except in the 1 instance in which the inversion occurred in all leads, the T wave in the opposite lead was upright and tended to be increased in amplitude.

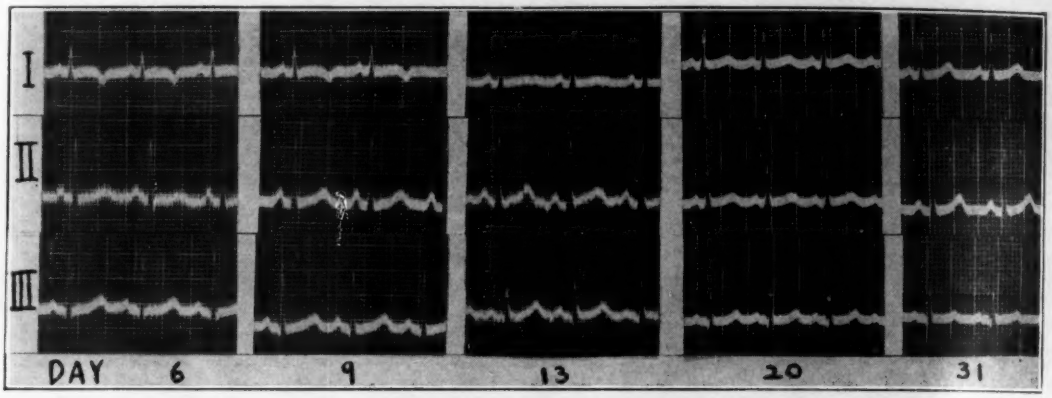

Fig. 7.—Electrocardiograms of a girl aged 4 years, with a 16 per cent increase in weight due to edema, cardiac enlargement, a large, tender liver and a maximum blood pressure 170 systolic, 122 diastolic. The patient received sulfanilamide from the fifth to the fourteenth day.

Late inversion of the T wave in lead I on the sixth and ninth days; double-peaked T in lead I on the thirteenth day. (The first three tracings in each lead were taken on an electrocardiograph with a string galvanometer; the last two on an oscillograph type of instrument. Standardization was similar in all tracings, but the speed of movement of the beam was less than that of the string.)

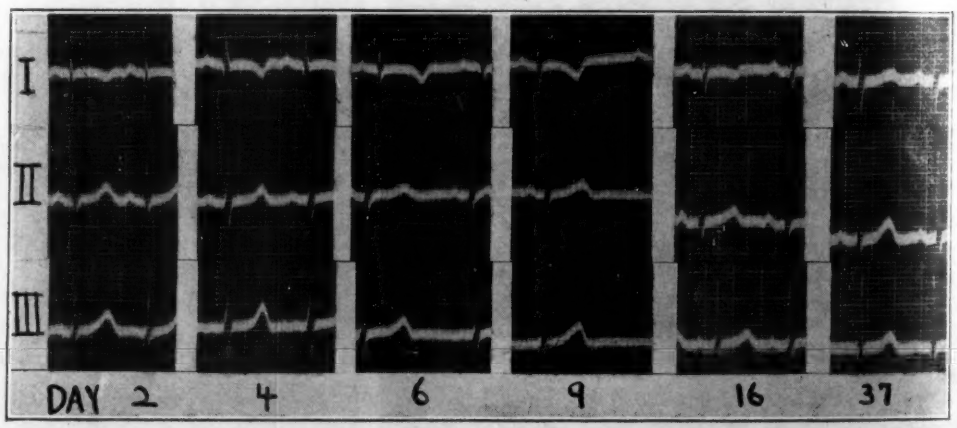

Fig. 8.—Electrocardiograms of a boy aged 5 years, with the heart and liver enlarged, gallop rhythm, a 12 per cent increase in weight due to edema and a maximum blood pressure of 150 systolic, 130 diastolic. The patient received magnesium sulfate on the second and third days and digitalis on the third and fourth days (2½ grains per 10 pounds followed by 1 grain daily for ten days).

Decreased amplitude of QRS in early tracings. Late inversion of T wave in lead I from second to sixteenth day inclusive with reciprocal elevation of the T wave in lead III; slight depression of ST in lead from the second to the ninth day inclusive; increased amplitude of Q in lead I, and of S in leads II and III on the fourth day; increased amplitude of S in leads I and II on the ninth day; prominent S in lead I still present on the thirty-seventh day.

edema or the administration of sulfanilamide may be implicated as a causative factor.

Transient inversion of T waves (figs. 1, 3, 4, 5, 6, 7 and 8) was noted in the tracings of 23

All children with negative T waves in lead I in their electrocardiograms had shown a considerable degree of hypertension on admission to the hospital, although the blood pressure in some

instances had begun to fall when inversion of the T wave first made its appearance. Inversion of the T wave in lead I was first noted at intervals varying from one to thirteen days after the onset of the disease, and it disappeared as early as the tenth day in 1 patient but was still present as late as the thirty-seventh day in another. Transient inversion of the T wave in lead III in at least 2 cases seems to have been the result of change in position of the heart, since it was associated with shift of the axis to the left. It is possible that even in tracings showing no deviation of the axis to the left transient inversion of the T wave in lead III may have been due to upward displacement of the heart. Serial roentgenograms of the chests of children ill with acute glomerulonephritis not infrequently show elevation of the diaphragm in the films taken early in the course of the illness. On the whole, children whose tracings showed transient negative or diphasic T waves in lead III were not so ill as those whose electrocardiograms showed negative T waves in lead I (table 3). As in lead I, the peak of the changes in the T wave in lead III did not always coincide with the period of most evident clinical symptoms and of greatest hypertension.

Upright T waves in lead III which were succeeded by diphasic or inverted waves in later tracings were noted 8 times. With the appearance of inversion in lead III the T waves in lead I tended to become increased in amplitude. High, sharply angulated T waves such as were reported by Master[2b] were observed 4 times (fig. 5). A moderate, transient increase in amplitude of T waves occurred in the tracings of 12 additional children. There were 4 instances of prolongation of the QT interval.

Depression of the ST interval never reached an amplitude greater than 1 mm. Definite sagging of lesser degree did appear as a transient phenomenon in the electrocardiograms of 14 children (table 2; figs. 1, 4, 6 and 8).

Incidence of Electrocardiographic Variations.—In the case of only 1 child were no changes observed in a series of tracings. If we eliminate variations that might be related to the presence of edema (low voltage of R, T and P), physiologic factors (relation of P wave to rate or sinus arrhythmia), to shift in position of the heart (inversion of T wave in lead III, with deviation of the axis to the left) or the administration of drugs, there still remain transient variations in serial electrocardiograms taken during the course of an attack of acute glomerulonephritis in 36 children (72 per cent) (table 5). It is to be emphasized that single tracings would in many instances have been interpreted as within normal limits, abnormalities being recognized only by the appearance of progressive changes in subsequent tracings. Such progressive changes appeared in the electrocardiograms of some children who presented no clinical signs of cardiac involvement. Conversely, an occasional child with definite indications of cardiac failure presented no significant electrocardiographic variations. In general, clinically recognizable cardiac involvement and abnormalities in the electrocardiogram were encountered most frequently in patients who had elevated blood pressures (table 4).

TABLE 2.—*Abnormalities of T Wave and ST Segment in 50 Cases of Acute Glomerulonephritis*

Leads	Low T*	Inverted T	Depressed ST	Prolonged QT
I	3	9	..	..
II	..	..	..	4
I and II	6	..	10	..
II and III	2	1	3	..
I, II and III	2	1	1	..
III	..	10†	..	..

* Excluding 10 cases possibly due to edema, and 8 occurring during the administration of sulfanilamide.
† Excluding 2 cases in which inversion of T waves occurred in relation with transient deviation of the axis to the left.

TABLE 3.—*Clinical Status of Patients Who Showed Inversion of the T Wave in Lead I as Compared with Patients Who Showed Inversion of the T Wave in Lead III*

	Negative T_1		Negative T_3	
	No.	%	No.	%
Cardiac involvement clinically	7	70	4	40
Large liver	5	50	3	30
Digitalis administration	6	60	2	20
Average maximum blood pressure	158/117		136/94	
Average maximum blood urea nitrogen	30 mg./100 Cc.		30 mg./100 Cc.	
Total number of cases	10		10	

TABLE 4.—*Relation of Clinically Recognizable Cardiac Involvement and Electrocardiographic Variations to Hypertension*

Maximum diastolic pressure:	Number of Patients	Patients with Cardiac Involvement Clinically		Patients with Electrocardiographic Variations	
		No.	%	No.	%
80 or below	13	1	8	6	46
100 to 81	8	2	25	6	75
120 to 101	18	11	62	15	83
Over 120	11	8	73	9	82
Total	50	22	44	36	72

COMMENT

A review of published observations on the variations in serial electrocardiograms obtained from patients ill with acute glomerulonephritis impresses one with the high incidence of abnormalities noted (in 60 to 100 per cent of the cases [table 5]. These changes are progressive, reversible, and apparently without significance so far as the ultimate cardiac prognosis is concerned.

Arrhythmias are rarely present. Defects in conduction are unusual. Abnormalities of the QRS complex, slurring or notching, increased depth of Q or S and increased duration, are pathognomonic of acute glomerulonephritis and stressed the absence of deviation of the ST segment and of changes in the Q wave as features which differentiated that condition from infarction of the anterior wall of the heart. In 2 of their cases there was transient inversion of the T wave in lead III. The significance of inversion of the T wave in the third lead has been stressed by Garreton.[2e] Illustrations of such inversion, isolated or associated with inversion of the T wave in lead II, are presented in the papers of Cossio [2f] and Williams.[2g] Reversible inversion of the T wave in lead III was also noted in the present series (figs. 1, 3, 5 and 6).

TABLE 5.—*Electrocardiographic Abnormalities in Acute Glomerulonephritis* *

	Tur [2a] Leningrad 1935	Master et al. New York 1936 [2b] 1937 [2c]	Langendorf and Pick [2d] Prague 1937 *	Garreton et al.[2e] Chile 1938	Cossio et al.[2f] Buenos Aires 1939	Williams [2g] Baltimore 1939	Ash et al. Present series Philadelphia 1943 †
Number of patients	13‡	24	12 ‡	36	30 ‡	15	50
Age in years	25-38	13-45 Average 27	15-43	14-50	4-13 Average 8	13-60 Average 29	½-13 Average 6.3
Average number of electrocardiograms	3.4	7	—	2	—	5.7	5.9
EKG variations	10; 77%	19; 79%	12; 100%	34; 94%	18; 60%	10; 66%	36; 72%
Arrhythmias, excluding sinus arrhythmia	1	4	0	0	—	0	1
Abnormalities of P wave	0	4	—	5	3	0	4
Prolonged PR	0	0	—	0	1	2	0
Low voltage	5	2	—	—	—‖	—	3
Right axis deviation	2	0	1	4 §	—‖	2	2
Left axis deviation	5	3	1	19 §	—‖	0	7
Abnormalities of QRS	0	2	—	24	17	1	11
High T	1	4	1	—	—	0	4
Low T	9; 70%	9; 37%	8; 67%	—	17; 57%¶	4; 27%	13; 26%
Diphasic or inverted T	8; 61%	8; 33%	12; 100%	27; 75%#	—	3; 20%	21; 42%
Leads I, II and III	2	0	0	0	—	1	1
Leads I and II	2	5	0	18 #	—	1	0
Lead I	3	1	11	—	—	0	9
Leads II and III	0	0	0	—	—	1	1
Lead II	0	2	0	—	—	0	0
Lead III	1	0	2	9	—	0	10
Prolonged QT	—	—	—	11	1	1	4
Depressed ST	—	—	—	6; 17%	8; 27%	—	14; 28%
Leads I, II and III	—	—	—	—	—	—	1
Leads I and II	—	—	—	—	7	—	10
Leads II and III	—	—	—	—	1	—	3
Low or absent initial positive deflection, precordial lead	—	3	—	—	—	2	—
Negative T, precordial lead	—	5	1	—	—	5	—

* So far as could be determined from the published reports, persistent changes have been excluded.
† Variations seemingly due to drugs or physiologic factors were excluded.
‡ Not all cases were first attacks of glomerulonephritis.
§ May not all be transient.
‖ Included in abnormalities of QRS.
Includes "low or inverted T_1 or T_2."
¶ "T wave alterations."

not mentioned at all by some authors and yet were noted in 67 per cent of the cases seen by one observer.[2e] Transient deviation of the electrical axis, most often to the left, was observed in a small percentage of cases by all. Depression of the ST segment was mentioned by two authors and occurred in about one fourth of the cases in the present series.

All observers have stressed the high proportion of changes in the T wave. These changes usually consist of lowering of amplitude, to the point of inversion in many instances. It so happened that in 11 of the 12 cases observed by Langendorf and Pick [2d] negativity of a previously positive T wave occurred in lead I, associated in 1 instance with negative T waves in the precordial lead. They thought these changes to be

A tendency toward reciprocal heightening of the T wave in lead III when inversion occurred in lead I was described by Langendorf and Pick. Such increased amplitude of the T wave in lead III was also observed by us (fig. 8) together with a similar tendency to heightening of the T wave in lead I in the presence of inversion of the T wave in lead III. The occasional presence of high, pointed T waves (first mentioned by Master) was also noted (fig. 5).

Observations on the precordial lead have been infrequent. A low or absent initial positive deflection and a negative T wave have been reported. Recent tracings with precordial leads taken by us from children ill with acute glomerulonephritis were abnormal in 4 of 9 instances. A low initial upward deflection in lead CF_2,

negative T waves and high, pointed T waves in CF_4 were each present once. Double upward deflections in CF_2 were noted 3 times.

Previous writers have commented on the fact that electrocardiographic variations in acute glomerulonephritis sometimes reach their maximum after the acute stage of the disease has passed and may recede gradually over a period of weeks. This was characteristic of the present series also. Although variations were at times noted within the first week or even on the first day in which the existence of the disease was recognized, it was not uncommon for the initial tracing of a series to be normal and for the subsequent ones to show the development of abnormalities at a time when clinical improvement had become evident and hypertension was receding.

Lack of success in correlating electrocardiographic changes with clinically recognizable cardiac involvement,[11] degree of renal involvement[12] or hypertension[13] has been reported. On the other hand, a greater frequency of electrocardiographic changes in patients with cardiac insufficiency[14] and a definite correlation between alterations in the electrocardiogram and a rise of blood pressure[2d] have been described by other observers. In the present series, although certain persons presented inconsistent data, electrocardiographic changes were noted more frequently in children who showed clinical signs of cardiac involvement. Thus, 86 per cent of the tracings taken from the 22 children with clinical evidence of cardiac failure showed abnormal variations, while in the tracings taken from the 28 children with negative or questionable cardiac data, variations were noted in 57 per cent. The incidence of cardiac involvement that could be detected clinically and of electrocardiographic abnormalities was greatest among those children in whom the diastolic blood pressure was high. Irrespective of the blood pressure, however, variation in the electrocardiogram was encountered more frequently than clinically obvious heart disease.

Volhard attributed the sudden cardiac failure in acute nephritis to arterial hypertension, aggravated by the existence of hydremic plethora of the blood in cases in which little or no edema was present. The unlikelihood of a normal heart's failing under the stress of transient hypertension was pointed out by Master, with the reminder that such failure does not occur as a result of the sudden elevation of pressure which is associated with tumor of the adrenal medulla or with lead poisoning. In his original paper on acute dilatation of the heart in postscarlatinal nephritis, Goodhart postulated that two conditions probably take part in its production: (1) sudden peripheral obstruction to the circulation and (2) degenerative changes in the cardiac muscle secondary to the scarlatinal pyrexia. At present, agreement seems general that myocardial changes in acute glomerulonephritis of whatever origin condition the heart so that it fails under the stress of a hypertension of sudden development. Various factors may take part in the production of such myocardial changes: injury or spasm of the coronary vessels, retention of fluid with resultant edema of the heart muscle, toxemia resulting from bacterial infections and the accumulation of metabolic products in the blood due to oliguria. Whether the resultant pathologic changes in the myocardium are in themselves sufficient to produce the electrocardiographic variations noted so frequently in acute glomerulonephritis is problematic. The high tolerance to digitalis observed in the patients of the present series would suggest that the myocardial injury is either qualitatively or quantitatively different from that which occurs in rheumatic infection, for instance.

Langendorf and Pick, on the basis of what they thought to be the characteristic pattern of acute glomerulonephritis with negative T waves in lead I, postulated a local change in the left ventricle, due to sudden overstrain following an acute rise in blood pressure. Cossio stressed the association of a depressed, upward bowed ST segment with negative T waves in some of his tracings and pointed out the resemblance to the deviations in the ST segment and in the T wave that have been described in the presence of predominant strain of either the right or the left ventricle.[15] He thought it probable that depression of the ST segment in leads I and II with a negative T wave in lead I was the result of dilatation of the left ventricle due to the sudden strain of a rapidly developing hypertension on an impaired myocardium. Similar changes in leads II and III would occur in association with predominant dilatation of the right ventricle.

Theoretically one would expect failure of the left ventricle to be primary in acute nephritis, since this ventricle would first be subjected to

11. (*a*) Master and Dack.[2b] (*b*) Master, Jaffe and Dack.[2c] (*c*) Langendorf and Pick.[2d] (*d*) Williams.[2g]

12. (*a*) Langendorf and Pick.[2d] (*b*) Williams.[2g]

13. (*a*) Master and Dack.[2b] (*b*) Master, Jaffe and Dack.[2c] (*c*) Cossio, Arana and Kreutzer.[2f]

14. (*a*) Tur.[2a] (*b*) Garreton.[2e] (*c*) Cossio, Arana and Kreutzer.[2f]

15. (*a*) Selzer, A.: The Clinical Significance of Persistent Depression of the RS-T Segment in the Electrocardiogram, Am. Heart J. **16**:336, 1938. (*b*) Barnes, A. R.: Electrocardiographic Patterns: Their Diagnostic and Clinical Significance, Springfield, Ill., Charles C Thomas, Publisher, 1940.

the strain of a peripheral hypertension. Clinically the picture of left ventricular failure, cardiac enlargement, gallop rhythm, accentuation of the second pulmonic sound, dyspnea and pulmonary congestion is not uncommon. The presence of dilatation of the left ventricle at necropsy has been reported as characteristic by Goodhart and Volhard. In one of Goodhart's patients the left ventricle was so much dilated that "at the apex very little muscle was left and all the support derived from interlacing of the muscle trabeculae was done away with by their distention." Other authors on the contrary, have commented on the failure to observe gross anatomic and significant microscopic changes at necropsy.[16] The children in the present series in whose electrocardiograms inversion of T waves occurred in lead I all presented a high degree of hypertension, and the majority showed clinical signs of heart failure. Whether, as is postulated by Barnes,[15b] such variations in the T wave in lead I are the result of chemical and electrical changes associated with predominant fatigue of the left ventricle is a subject for speculation.

The existence of unequivocal right-sided failure in acute glomerulonephritis has been questioned.[2c] Volhard commented on the rapid development of enlargement of the heart and liver and engorgement of the peripheral veins in hypertensive patients with acute nephritis who presented little or no edema. Williams reported a rise of venous pressure in 9 of 11 patients on whom more than one determination had been made. Venous pressure was high (16 to 28 cm.) in the 5 children in the present series for whom it was determined. Enlargement of the liver and engorgement of the veins were present in all 5 children. In 1 of the 4 reports of necropsy presented by Goodhart there is mention of "overdistention" of the right side of the heart as well as of dilatation of the left ventricle. Theoretically one would expect distention of the right ventricle to follow the pulmonary engorgement resulting from left ventricular failure. If such were the case, and if inversion of the T waves in leads III and II reflected the physicochemical changes associated with predominant dilatation of the right ventricle, patients with transient negativity of the T waves in lead III might be expected to be more critically ill than those with transient inversion of the T waves in lead I. Actually the reverse was true in the present series, the incidence of heart failure being greater among those with predominant variations in lead I. In some instances isolated inversion of the T waves in lead III was most probably related to change in position of the heart due to elevation of the diaphragm. Elevation of the diaphragm is not infrequently observed in roentgenograms of the chest taken early in the course of acute glomerulonephritis.

16. (*a*) Master, Jaffe and Dack.[2c] (*b*) McIntosh, R.: Circulatory Failure in Acute Glomerulonephritis, Canad. M. A. J. **46**:445, 1942.

SUMMARY

An analysis of the variations in serial electrocardiograms obtained from 50 children ill with a first attack of acute glomerulonephritis disclosed abnormalities in 72 per cent of the group. Abnormal variations were present in the tracings of 86 per cent of the children with clinical signs of heart failure and in 57 per cent of those with negative or questionable cardiac findings. The incidence of clinically recognizable heart disease and of electrocardiographic variations was greater among patients in whom the blood pressure was high. At all levels of blood pressure, abnormalities in the electrocardiogram were noted more frequently than clinical evidences of cardiac involvement.

The most striking changes were observed in the T wave, consisting chiefly of flattening and inversion in one or more leads, although a transient increased amplitude of the T wave was also occasionally observed. Inversion of the T wave occurred late in the cycle and was not infrequently preceded, especially in leads I and II, by a slightly depressed, upward bowed ST segment. Transient inversion of the T wave occurred as frequently in lead III as in lead I. The incidence of heart failure, however, was greater in association with inversion of the T wave in lead I than in association with inversion of this wave in lead III. In some instances isolated transient inversion of the T wave in lead III may have been related to elevation of the diaphragm and change in position of the heart.

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Case Reports

TETANY DUE TO DEFICIENCY IN MAGNESIUM

ITS OCCURRENCE IN A CHILD OF SIX YEARS WITH ASSOCIATED OSTEOCHONDROSIS OF CAPITAL EPIPHYSIS OF FEMUR (LEGG-PERTHES DISEASE)

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MEDICAL CORPS, ARMY OF THE UNITED STATES

In 1932 Kruse, Orent and McCollum [1] induced tetany in rats and dogs by feeding them a diet free of magnesium. Sjollema and Seekles [2] discovered that calves reared on whole milk, which is low in magnesium, frequently showed severe symptoms of tetany, accompanied with low values for the plasma magnesium. Sjollema also described "grass tetany," a disease occurring spontaneously in cattle, characterized by severe tetanic symptoms and low blood magnesium.

This form of tetany, however, is not generally recognized as occurring in human beings; Best and Taylor [3] in 1939 stated that it had not been reported in the human subject. In a search of the available literature, however, reports were found of a few cases which might fit this classification. Denis and Talbot [4] reported several cases of tetany in patients showing low values for plasma magnesium. Hirschfelder and Haury [5] listed 10 cases of convulsions and twitching and a low plasma magnesium. Unfortunately, few clinical data are given in either of these communications.

The term tetany should be retained in its original physiologic and clinical sense, to refer to a syndrome characterized by various symptoms and signs indicating a generalized hyperirritability of the nervous system, such as muscular cramps, carpopedal spasm, Chvostek's sign and, in infants and young children, laryngeal stridor. Erb's reactions to electric stimulation show in the most direct form the nervous hyperirritability and are of great value in diagnosis of tetany in a young subject. A patient showing these signs, regardless of the blood chemistry, has tetany.

The establishment of a normal value for plasma magnesium has been a problem of some scope. Haury and Cantarow,[6] using the largest series of subjects reported, established 1.7 and 3.1 mg. per hundred cubic centimeters of plasma as the lower and upper limits of normality. Bogert and Plass [7] in a study of mothers and their newborn babies observed approximately the same normal values and also established the fact that there is no essential difference between babies and adults in the level of plasma magnesium. As to the critical level for tetanic symptoms, Kruse, Orent and McCollum [1] reported that in rats it was 1 mg. per hundred cubic centimeters. In a small series of tests done at this hospital to check the accuracy of our technic, the normal values for children tended to fall in the upper range of normal values as determined for adults.

The following case is of interest because the diagnosis of tetany was definitely established on the basis of intermittent and chronic manifestations by the criteria just mentioned; the plasma magnesium was so low that it could not possibly be considered normal; other causes of tetany, so far as possible, were ruled out, and the patient responded both clinically and chemically, to therapy with magnesium sulfate by mouth.

The values for plasma magnesium were determined by the method described by Briggs [8] and were carefully rechecked.

REPORT OF A CASE

The only son of a white officer in the United States Army was first admitted to Gorgas Hospital at the age of 7 months, because of repeated convulsions for a period of one month. He had healthy, normal parents, and there was no family history of epilepsy or other

1. Kruse, H. D., Orent, E. R., and McCollum, E. V., J. Biol. Chem. **96**:519, 1932; **100**:603 (May) 1933.
2. Sjollema and Seekles, cited by Kruse, Orent and McCollum.[1]
3. Best, C. H., and Taylor, N. B.. The Physiological Basis of Medical Practice, ed. 2, Baltimore, Williams & Wilkins Company, 1939.
4. Denis, W., and Talbot, F. B.: Calcium in Blood of Children, Am. J. Dis. Child. **21**:29 (Jan.) 1921.
5. Hirschfelder, A. D., and Haury, V. G.: Clinical Manifestations of High and Low Plasma Magnesium: Danger of Epsom Salt Purgation in Nephritis, J. A. M. A. **102**:1138 (April 7) 1934.
6. Haury, V. G., and Cantarow, A.: J. Lab. & Clin. Med. **27**:616 (Feb.) 1942.
7. Bogert, L. J., and Plass, E. D.: J. Biol. Chem. **56**:297 (June) 1923.
8. Briggs, A. P.: J. Biol. Chem. **59**:255 (March) 1924.

familial disease. He had been born by low forceps delivery after three days' labor, and immediately after birth the hands were noted to be flexed. Tetany of the newborn was diagnosed, and the baby was given lime in some form. It cannot be learned what the blood calcium was at that time, but in spite of the calcium given the child remained "nervous" and had frequent cyanotic attacks. When he was 6 weeks of age, roentgen examination of the chest is said to have disclosed a large thymus, and one roentgen ray treatment was given, after which the thymus was pronounced normal. However, the cyanotic attacks persisted, and a coarse tremor developed. Halibut liver oil with viosterol was given in daily doses of 12 drops from birth; the diet was evaporated milk, corn syrup (Karo) and water, with puréed foods started at 4 months, and calcium was given continuously from birth on.

The patient at 6 months of age began having frank convulsions almost daily, lasting three to four minutes, characterized by cyanosis, tonus and clonus.

Physical examination showed a fat, healthy-looking baby of 7 months, who did not appear to be abnormal. Roentgen examinations showed that there was no enlargement of the thymus and that the skull and long bones were normal. The blood plasma at this time contained 9 mg. of calcium per hundred cubic centimeters. The blood count, the Kahn reaction of the blood and the urine and stools were normal. A certain degree of shakiness and tremor was noted, but the convulsions gradually became less frequent. The patient's tremor persisted, and, while the case was being followed in the clinic, determinations of blood calcium were made at the ages of 10 months (10.6 mg. per hundred cubic centimeters) and 18 months (9.9 mg. per hundred cubic centimeters).

The patient was readmitted to the hospital at 3 years of age because of attacks of dizziness. Physical examination still failed to show abnormalities. His blood pressure, taken for the first time, was 90 systolic and 54 diastolic. The calcium content of the plasma at this age was 10.1 mg. per hundred cubic centimeters.

The patient continued to have a tremor but had no further convulsions until he was 3½ years of age, when he was readmitted to the hospital with a limp of the left leg. There was some atrophy of the left leg according to measurements, and a roentgenogram of the hip showed the typical picture of osteochondrosis of the capital epiphysis of the femur (Legg-Perthes disease), including fragmentation and flattening of the epiphysis. Routine tests of the blood, urine and stool gave negative results. The blood chemistry at the time of this admission showed: plasma calcium, 12.9 mg. per hundred cubic centimeters; nonprotein nitrogen, 36.1 mg., and dextrose (fasting), 66.1 mg.

For the next two years the patient was admitted frequently to the surgical service for the application of hip spicas. The course of the Legg-Perthes disease was not remarkable, following the usual sequence of epiphysial absorption, flattening and then slow regeneration.

At the age of 6 years the patient was readmitted to the medical service with an infection of the upper respiratory tract. An electrocardiogram taken at this time was normal. The boy continued to be generally well except for the tremor, which interfered with his learning to write legibly; his grade in writing was always D, although he received A or B in every other subject. He also had had evanescent attacks of slight dizziness, when he would turn pale around the mouth. The mother was somewhat troubled by the frequent cramps in his legs, but since they passed off with a little massage she attributed them to the Legg-Perthes disease. He had not had a frank convulsion since he was 1 year of age.

I saw the patient for the first time when, at the age of 6, he entered the hospital with an attack of tertian malaria. Treatment with quinacrine hydrochloride produced prompt subsidence of the fever and disappearance of parasites from the blood as shown by smears. At this time the child began to complain of cramps in the calf of the right leg. The patient got steadily worse, and within an hour he showed typical tetany. The hands were held in the "obstetric" position and the feet in the extended position of carpopedal spasm; the muscles of the arms and legs cramped and caused considerable pain. Chvostek's sign, however, was negative at this time. Blood taken [before treatment was given] was tested for calcium, dextrose and carbon dioxide–combining power, and the following results were later reported: dextrose 64 mg. per hundred cubic centimeters; calcium, 10.8 mg. per hundred cubic centimeters, and carbon dioxide–combining power, 50.2 volumes per cent.

Then 45 grains (2.91 Gm.) of ammonium chloride was given without inducing the slightest relief. A solution of calcium gluconate was administered intramuscularly and intravenously, still with no effect on the spasms. Unfortunately, magnesium sulfate was not tried. The pain and spasm subsided over a period of forty-eight hours. Erb reactions at this time showed a cathodal opening contraction with a current of less than 2 milliamperes. I believe that, in combination with the clinical symptoms, this is diagnostic of tetany. A more complete study of the blood chemistry, done after the subsidence of the tetanic attack, showed the following levels: nonprotein nitrogen, 24.2 mg. per hundred cubic centimeters; sodium chloride, 460 mg.; sodium, 320 mg.; potassium, 17.5 mg.; magnesium, 1.7 mg. and phosphorus, 3.3 mg. All these values are normal, but the magnesium is at the lowest level that is considered normal. The blood for these tests was not taken during the spasm. The observation was suggestive enough, however, to warrant magnesium therapy. The patient was sent home and was given 5 grains (0.3 Gm.) magnesium sulfate three times a day by mouth.

The symptomatic results were striking. The tremor and attacks of dizziness disappeared. The patient's grade in writing in school rose from D to B. Three weeks later the Erb reactions showed the cathodal opening contraction requiring a current of 5 milliamperes.

At this time the patient was taken on a trip and, unfortunately for him, the medicine was left at home. After about a week without the medicine, he had a recurrence of the tremor and severe cramps, one attack lasting all night. On returning to the Isthmus, the child was readmitted to the hospital, this time for a mild bacillary dysentery. He showed positive Trousseau signs and a positive Chvostek reaction bilaterally. The old tremor had returned. The blood now showed an unusually low magnesium content: plasma magnesium 0.6 mg. per hundred cubic centimeters, plasma calcium 11.2 mg. and plasma phosphorus 2.2 mg. The level for magnesium, I believe, is conclusively low. The laboratory checked the result by repetition of the test, and the technic was considered accurate. The patient was given magnesium sulfate, and the previously described benefits

resulted. The blood magnesium after two weeks therapy with 5 grains three times a day was 2.6 mg. per hundred cubic centimeters. The Legg-Perthes disease was almost healed already under orthopedic care; hence it was impossible to determine the effect of raising the plasma magnesium on the course of this illness.

COMMENT

There are several interesting aspects presented by this case: first, the relationship of the tetany to the low value for magnesium in the plasma; second, the clinical improvement and the simultaneous rise in plasma magnesium following administration of magnesium sulfate by mouth, and, third, the suggested relationship which might exist between low magnesium and osteochondrosis of the capital epiphysis of the femur.

I believe that the demonstration of the classic clinical signs and symptoms is diagnostic of tetany; the reservation of the term to specify any particular pattern in blood chemistry is considered presumptive. The next step is to rule out the other causes of tetany. The accompanying table excerpted from Best and Taylor [8] gives the generally accepted types of tetany, with the blood chemistry pattern associated with each. The first four types are ruled out in this case by the consistent presence of a normal amount of calcium in the blood plasma; the last three, not only by the presence of normal carbon dioxide–combining power but by the absence of vomiting of bicarbonate ingestion, and of overbreathing. The normal values for chlorine and phosphorus rule out phosphate tetany. With these classic causes of tetany ruled out the occurrence of low plasma magnesium in a patient with tetany is highly suggestive of a causal relationship between the two, in view of the fact that such a relationship has been previously demonstrated in animals.

Blood Chemistry Pattern Associated with Different Types of Tetany *

	Calcium	Bicarbonate	Chloride	Phosphorus
Infantile (rachitic)	Reduced	Normal	Normal	Normal or reduced
Tetany of osteomalacia	Reduced	Normal	Normal	Normal or reduced
Parathyroid tetany	Reduced	Normal	.....	Increased
Phosphate tetany	Reduced	Normal	Normal or increased	Increased
Gastric tetany	Normal	Increased	Reduced	Increased
Bicarbonate tetany	Normal	Increased	Reduced	
Hyperpneic tetany	Normal	Increased		

* Excerpted from Best and Taylor.[8]

Although Hirschfelder and Serles [9] by administration of magnesium sulfate by mouth to normal men obtained a maximum increment in the plasma of only 0.41 mg. per hundred cubic centimeters in spite of the fact that from 40 to 44 per cent was absorbed, I was able to obtain an increment of 2 mg. per hundred cubic centimeters in this patient. Since the kidneys were normal in both instances, it can only be presumed that it is easier to raise the value from a pathologically low level than from a level originally normal. Further investigation is necessary to clarify this point.

I have been unable to find reports of any studies on the relationship between low plasma magnesium and osteochondrosis of the capital epiphysis of the femur. Haury and Cantarow,[6] in their series of determinations of the magnesium content of the plasma under normal and under pathologic conditions, included 2 cases of fracture with nonunion in which the plasma magnesium values were low. This problem is beyond the scope of this communication, but it is now under investigation.

CONCLUSIONS

Clinical tetany, apparently caused by a low plasma magnesium content, occurred in a child of 6 years who also had osteochondrosis of the capital epiphysis of the femur (Legg-Perthes disease). A significant rise in the content of magnesium in the blood plasma, with a concomitant improvement in the nervous hyperirritability, was obtained by giving repeated doses of magnesium sulfate by mouth.

J. C. Jacob, B.S., gave technical assistance.

9. Hirschfelder, A. D., and Serles, E. R., cited by Hirschfelder and Haury.[5]

RELAPSING FEBRILE NODULAR NONSUPPURATIVE PANNICULITIS (WEBER-CHRISTIAN DISEASE)

REVIEW OF THE LITERATURE, WITH REPORT OF A CASE

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Relapsing febrile nodular nonsuppurative panniculitis (Weber-Christian disease) is characterized by recurring bouts of fever, associated with the appearance of crops of nodules, varying from the size of a pea to several centimeters in diameter, usually on the thighs and arms, frequently on the abdomen and back and occasionally on the lower part of the legs. The nodules, which may be either painless or somewhat tender to touch, are erythematous and raised above the surface of the normal skin. Over a period of a few months they slowly regress, leaving shallow or deep pitted areas covered by normal skin. Twenty-seven cases have been reported, the majority of the patients being adults, 22 women and girls and 5 men. The 4 children with the disease previously reported on have been girls[1] 8 to 11 years of age, and their illness lasted two to twelve months. The case presented is the first to be reported in which this condition has occurred in a boy, and the patient is the youngest described in the literature.

REPORT OF CASE

A 23 month old white boy was admitted to the babies' wards of the New York Post-Graduate Medical School and Hospital on Jan. 11, 1943. Three months earlier the patient's parents had noticed what they considered to be a "swelling" of the legs, gradual in onset. This swelling slowly increased, and small ridges were noted to extend across the dorsum of each foot. There was no pain or loss of function; the patient was active and not bothered by the condition. No fever or ill health was noted in this period. No contributory factors appeared in the patient's history or in the family history.

Physical Examination.—The patient was slender and moderately well developed and did not appear to be ill. The only significant physical signs were small, "shotty" inguinal nodes, circumscribed erythematous areas on the anterior aspects of both thighs and the lesions about the ankles. There was on each ankle a symmetric atrophy of the subcutaneous tissues in a semicircular area extending for an inch in every direction from the external malleolus. This atrophy also extended forward to include the dorsum of the foot and ankle and, on the right foot, the mesial aspect below the internal malleolus, down to but not including the plantar surface. The normal tissue was sharply demarcated from the atrophic by a hard rolled border which was erythematous but not warm or tender (fig. 1.). The atrophic area was pigmented more deeply than the surrounding normal skin.

Laboratory Data.—Roentgenographic examination of the ankles and feet on Jan. 13, 1943 showed no gross osseous or articular abnormality. A faint reticulation and deep subcutaneous thickening of the soft tissues were observed in the lower part of the legs and over the dorsa of the feet.

Fig. 1.—Photograph of the ankles, showing atrophy and a rolled border demarcating normal from atrophic skin.

The urine was normal. There were 4,310,000 red cells per cubic millimeter of blood and 6,900 white cells; of the white cells, 54 per cent were polymorphonuclear leukocytes, 5 per cent eosinophilic leukocytes, 39 per cent lymphocytes and 2 per cent monocytes. The blood contained 11 Gm. of hemoglobin, 20 to 22 mg. of urea nitrogen, 39.5 mg. of nonprotein nitrogen and 275 mg. of cholesterol (145 mg. as esters) per hundred cubic centimeters. The content of lipase in the blood was normal. The erythrocyte sedimentation rate was 15 mm. in one hour. Negative results were obtained from a Wassermann test of the blood and from a Mantoux test (tuberculin 1:10,000).

Biopsy.—A specimen for biopsy was taken from the lesion over the right ankle, including normal tissue, the rolled border and atrophic tissue down to the muscle. The specimen thus obtained consisted of a thin slice of

From the Departments of Pediatrics and Pathology, New York Post-Graduate Medical School and Hospital, Columbia University.

1. (*a*) Gilchrist, T. C., and Ketron, L. W.: A Unique Case of Atrophy of the Fatty Layer of the Skin, Preceded by the Ingestion of the Fat by Large Phagocytic Cells—Macrophages, Bull. Johns Hopkins Hosp. **26**: 291-294 (Oct.) 1916. (*b*) Cummins, L. J., and Lever, W. F.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), Arch. Dermat. & Syph. **38**:415-426 (Sept.) 1938. (*c*) Hazel, O. G., and Lamb, J.: Primary Panniculitis (Weber-Christian Disease), J. Oklahoma M. A. **33**:1-5 (Jan.) 1940.

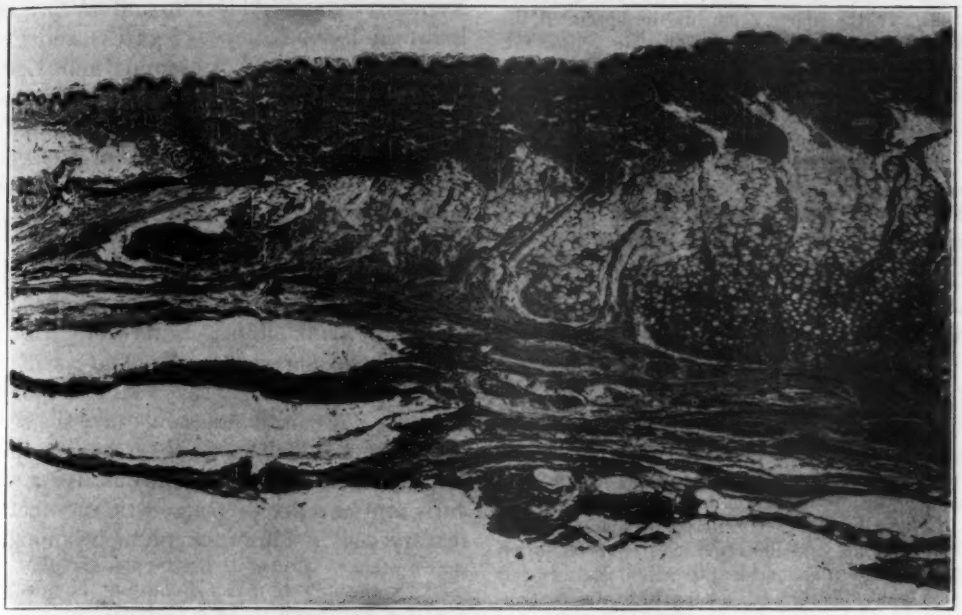

Fig. 2.—Low power view of a section of skin and subcutis from the margin of the lesion, showing the inflammation in the fat on the right and the resultant atrophy on the left.

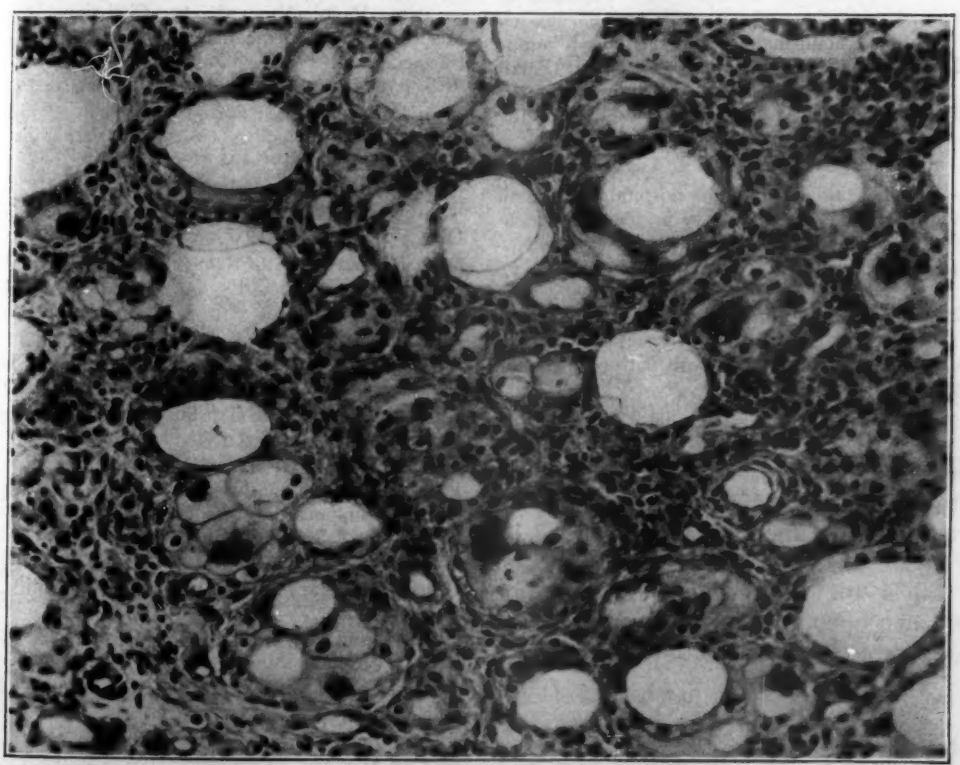

Fig. 3.—High power view of the inflammation in the subcutis, showing the absence of suppuration and the presence of numerous macrophages with foamy cytoplasm ("lipophages").

skin and subcutis 37 mm. long, 5 mm. broad and 11 mm. thick. The cutaneous surface was finely wrinkled and gray and without discernible lesions. The cutis appeared to be normal. In the upper 2 cm. of the specimen the subcutis was filled with lobules of soft, pale yellow fat. This fatty layer ended abruptly in a rounded border, and the subcutis of the remainder of the specimen was composed of delicate gossamer sheets of fibrous tissue entirely devoid of fat. At the point of transition no signs of inflammation were discerned.

Microscopic examination of the epidermis and dermis did not reveal any abnormality, but there were profound changes in the subcutis associated with disappearance of the fat. At one end of the specimen the subcutis was composed of normal adipose tissue presenting lobules of mature cells filled with fat, separated by delicate fibrous septums, while at the other end the subcutis was composed of fibrous tissue devoid of fat. In the intervening zone there was a noncircumscribed area of panniculitis, in which there was necrosis, and disappearance of fat associated with a polymorphous cellular infiltration. The predominating cells were large mononuclear phagocytes with extensively vacuolated (fat-filled) cytoplasm. Some of these cells were multinucleated. These lipophages occurred in sparse groups between the fat cells, and in larger aggregations, often in mosaic pattern, replacing the fat cells. No crystals of fatty acid were identified. There was also a haphazard infiltration by lymphocytes, plasma cells and a few eosinophilic leukocytes. The trabeculae were thickened by fibrosis. In the zone in which the fat had been replaced by fibrous tissue perivascular infiltrations remained. Numerous small vessels were surrounded by compact infiltrations of macrophages containing fat, lymphocytes, plasma cells and fibroblasts. The only additional abnormality observed was a minor degree of endothelial proliferation in a single small artery in the otherwise normal fat proximal to the lesion. The inflammation did not have any specific features. These changes conform to those described as occurring in Weber-Christian disease (figs. 2 and 3).

Course.—During eight days in the hospital the patient was asymptomatic except for a rise in temperature to 102 F., which lasted about eight hours.

Since the boy was discharged from the hospital, Jan. 18, 1943, there has been no progression of the lesions of the ankles and feet and no new lesions have appeared. He was seen again in June 1943. All signs of inflammation had disappeared, leaving only atrophy of the subcutaneous tissues of the ankles.

DISCUSSION

Twenty-seven cases of febrile nodular nonsuppurative panniculitis have been reported in the literature. The first case was described by Pfeifer [2] in 1892; the second by Gilchrist and Ketron [1a] in 1916. Weber [3] applied the name "relapsing nonsuppurative nodular panniculitis" in his case, and to this Christian [4] properly added the adjective "febrile" in reporting the fourth case in 1928. Other cases were reported by Netherton [5] and Alderson and Way [6] in 1933, Brill [7] in 1936, Bailey [8] (5 cases) and Reed and Anderson [9] in 1937, Cummins and Lever [1b] in 1938, Binkley [10] in 1939, Tilden, Gotshalk and Avakian,[11] Hazel and Lamb,[1c] Skiöld [12] and Hartwell and Thannhauser [13] in 1940, Hanson and Fowler [14] and Larson and Ootkin [15] in 1941 and Rosenberg and Cohen [16] in 1942.

Variations from the typical clinical picture have been noted in reports of isolated cases. Keil [17] proposed a classification of these various forms of panniculitis. Sundwall [18] described a patient who showed localized areas of atrophy in the left femoral (Scarpa's) triangle, without evidence of inflammation or the previous presence of nodules. Biopsy showed absence of fat, sclerosis of the subcutaneous tissue, a normal cutis and absence of phagocytic or other inflammatory cells. This case might be thought of as

2. Pfeifer, V.: Ueber einen Fall von herdweiser Atrophie des subcutanen Fettgewebes, Deutsches Arch. f. klin. Med. **50**:438-449, 1892.

3. Weber, F. P.: A Case of Relapsing Nonsuppurative Nodular Panniculitis, Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, Brit. J. Dermat. **37**:301-311 (July) 1925.

4. Christian, H. A.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Int. Med. **42**:338-351 (Sept.) 1928.

5. Netherton, E. W.: Relapsing Nodular Nonsuppurative Panniculitis, Arch. Dermat. & Syph. **28**:258-259 (Aug.) 1933.

6. Alderson, H. E., and Way, S.: Relapsing Febrile Nonsuppurative Panniculitis (Weber), Arch. Dermat. & Syph. **27**:440-449 (March) 1933.

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12. Skiöld, N.: Relapsing Febrile Nonsuppurative Panniculitis, Acta med. Scandinav. **105**:43-47, 1940.

13. Hartwell, A. S., and Thannhauser, S. J.: Case Presentation and Discussion of Relapsing Febrile Nodular Nonsuppurative Panniculitis, Bull. New England M. Center **2**:362-368 (Dec.) 1940.

14. Hanson, W. A., and Fowler, L. H.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Minnesota Med. **24**:779-782 (Sept.) 1941.

15. Larson, C. P., and Ootkin, B. N.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian's Disease), Am. J. Clin. Path. **11**:781-787 (Oct.) 1941.

16. Rosenberg, W. A., and Cohen, T. M.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Illinois M. J. **81**:59-62 (Jan.) 1942.

17. Keil, H.: Panniculitis: Its Place in Nosology, Brit. J. Dermat. **47**:512-521 (Dec.) 1935.

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one in which only the end result of panniculitis was evident, with no history of a previous acute inflammatory process. Shaffer [19] reported, under the title "Liquefying Nodular Panniculitis," the case of a 33 year old woman who had attacks of fever for twelve years, associated with the appearance of crops of nodular lesions on all extremities. Despite the fact that many of these nodules liquefied, formed cysts and ruptured spontaneously, this should be considered a case of Weber-Christian disease because it had all the typical characteristics plus the added feature of spontaneous rupture of the cysts containing the liquefied fat. (The liquefaction of fat has been noted in other typical cases of Weber-Christian disease.) Weber's [20] second patient, a 53 year old man with tertiary syphilis, had fever and crops of nodules on the arms and thigh after treatment with potassium iodide. Some of these nodules discharged sterile pus. The lesions disappeared when the iodide medication was discontinued and recurred when it was resumed. A biopsy was not made. Weber pointed out, in conclusion, "that iodides (or bromides?) may, in certain rare idiosyncratic individuals, give rise to a syndrome resembling relapsing febrile nodular nonsuppurative panniculitis, and that in one or two of the nodules the panniculitis may proceed to suppuration." All these cases have had one major feature in common, involvement of subcutaneous fat alone, but this feature may also be found in other conditions in which it plays a minor role; Weber and Gray [21] reported a case in which there were inflammatory changes in the muscle as well as in the subcutaneous fat, and which they therefore called an instance of "polydermatomyositis."

The lesions may be widespread, but they occur most frequently on the arms and thighs, often on the legs and trunk. Any particular patient may show single or multiple lesions. In 1 case [1b] the soles were involved. Only the hands have been spared in all cases. The distribution of lesions in all reported cases is noted in table 1.

Death occurred in 2 cases,[22] in one of which an autopsy was performed [11]; pulmonary and disseminated tuberculosis was the cause of death but no other lesions similar to those of the subcutaneous fat could be found.

19. Shaffer, B.: Liquefying Nodular Panniculitis, Arch. Dermat. & Syph. **38**:535-544 (Oct.) 1938.

20. Weber, F. P.: A Further Note on Relapsing Febrile Nodular Nonsuppurative Panniculitis, Brit. J. Dermat. **47**:230-233 (June) 1935.

21. Weber, F. P., and Gray, A. M. H.: Chronic Relapsing Polydermatomyositis with Predominant Involvement of Subcutaneous Fat (Panniculitis), Brit. J. Dermat. **36**:544-560 (Dec.) 1924.

22. Bailey.[8] Tilden, Gotshalk and Avakian.[11]

The specificity of the clinical syndrome is not reflected in the histologic changes observed and described,[23] although these have been fairly uniform. Similar inflammatory lesions in subcutaneous fat with subsequent atrophy occur in diseases with totally different clinical features.[8] The observations suggest that a subtle change occurs in the fat, accompanied by an inflammation whose chief feature is removal of the fat by phagocytosis without visible hydrolysis. Whether the inflammation initiates the process or is the result of the changes in the fat is not clear. Pathologic studies have not established a pathognomonic histologic picture, elucidated the pathogenesis or illuminated the etiology.

Laboratory Data.—In addition to biopsy of the lesions, numerous laboratory tests have been carried out in the cases reported in the literature. Leukopenia was found in 3 cases,[24] severe leukocytosis in 2,[25] moderate leukocytosis in 2 [26] and a normal leukocyte count in others.[11] Tests of the blood gave negative results for Brucella,[27] as they did also for typhoid, paratyphoid and dysentery.[28] The basal metabolic rate was normal in some cases [7] and low in 1.[1c] Roentgenograms of the long bones of several patients revealed no abnormalities.[29] The chemistry of the blood, including the contents of cholesterol and lipids,[12] was within normal limits.[30] Cultures of the blood consistently gave negative results, and no organisms could be found in stained sections taken from active lesions.[29] The erythrocyte sedimentation rate determined in 2 cases [31] was found to be increased. Sternal marrow, obtained by puncture, was normal.[7] Review of these numerous laboratory tests reveals that they shed no light on the causation or course of the condition nor do they establish diagnostic criteria.

Etiology.—The cause of relapsing febrile nodular nonsuppurative panniculitis is unknown, but focal infections,[32] and iodides and bromides [33] have been suggested as causes. Stockman [34]

23. Gilchrist and Ketron.[1a] Weber.[3] Christian.[4] Bailey.[8]

24. Christian.[4] Brill.[7] Bailey.[8]

25. Gilchrist and Ketron.[1a] Pfeifer.[2]

26. Pfeifer.[2] Hazel and Lamb.[1c]

27. Christian.[4] Alderson and Way.[6] Brill.[7] Bailey.[8]

28. Christian.[4] Alderson and Way.[6]

29. Gilchrist and Ketron.[1a] Pfeifer.[2] Weber.[3] Christian.[4]

30. Gilchrist and Ketron.[1a] Cummins and Lever.[1b] Christian.[4] Brill.[7]

31. Cummins and Lever.[1b] Skiöld.[12]

32. Pfeifer.[2] Stockman.[34]

33. Bailey.[8] Binkley.[10]

34. Stockman, R.: British Medical Association Lectures on Chronic Muscular Rheumatism and Panniculitis, Brit. M. J. **1**:293-295 (Feb. 25) 1928.

TABLE 1.—*Clinical Features of Reported Cases of Weber-Christian Disease*

Author	Duration, Yr.	Year	Age, Yr.	Sex	Pain	Fever	Distribution of Lesions						Secondary Atrophy	Focal or Systemic Infections	Drugs
							Arms	Abdomen	Back	Thighs	Legs	Other Parts			
Pfeifer	2	1892	23	F	..	+	+	+	+	+	+	.....	+		
Gilchrist	1/2	1916	8	F	..	+	..	..	..	+	+	.....	+		
Weber	1/10	1924	50	F	..	+	+	..	+	+	+	.....	..	.....	Bromides
Christian	10	1928	32	F	..	+	+	+	+	..	+	.....	+		
Netherton	1	1933	46	F	+	+	..	..	..	..	+	.....	+		
Alderson	15	1933	41	F	+	+	+	..	..	+	+	.....	+	Dental caries	
Weber	1/12	1935	53	M	..	+	+	..	..	+	..	.....	..	Syphilis	Iodides
Brill	3	1936	19	F	+	+	+	+	..	+	..	.....	+	Tonsillitis, dental caries	
Bailey	1/3*	1937	24	F	+	+	+	+	+	+	..	.....	+	Tonsillitis, dental caries	
	3/4	1937	43	F	+	+	+	+	..	+	..	.....	+	Tonsillitis, dental caries	Iodides
	3/4	1937	50	F	+	+	+	+	..	+	+	.....	+	Tonsillitis, dental caries	
	4	1937	38	M	..	+	+	+	..	+	+	.....	+	.....	Bromides
	10	1937	45	F	..	+	+	+	..	+	+	.....	+	Tonsillitis, dental caries	Iodides
Reed	9	1937	34	F	+	..	..	..	..	+	+	.....	+		
Cummins	1/6	1938	10	F	..	+	+	..	..	..	..	.....	+	Dental caries	
	1/2	1938	10	F	+	+	+	..	..	+	+	Feet	+	Dental caries	
Shaffer	12	1938	33	F	..	+	+	..	..	+	+	.....	..	.....	Iodides, bromides
Binkley	1/6	1939	36	F	..	..	+	..	..	..	+	Breast	..	Tonsillitis, dental caries	
Hazel	1	1940	11	F	..	..	..	..	..	+	+	.....	+		
Tilden	1/12*	1940	64	M	+	+	+	+	+	+	+	.....	+	Tuberculosis	
	1/12	1940	54	F	+	+	+	+	..	+	..	.....	..	Dental caries	
Skiöld	4	1940	51	F	+	+	+	..	..	+	+	.....	+	Dental caries	
Hartwell	2	1940	32	F	..	+	+	+	+	..	..	Face	+	Pleurisy, pericarditis	
Hanson	1/4	1941	28	M	+	+	..	..	..	..	+	.....	+		
Larson	1/12	1941	58	M	+	+	+	+	+	+	..	.....	+		
Rosenberg	1/12	1942	38	F	+	+	..	..	..	..	+	.....	..	.....	Iodides, bromides
	1/30	1942	35	F	+	..									
Larkin	1/4	1943	1 11/12	M	..	+	..	..	..	..	..	..... Feet	+ +	Dental caries	Bromides

* The patient died.

has warned against placing this condition in the already too confused category of chronic rheumatism. Foci of infection were found in dental cavities and tonsils in several cases [35] but no such foci were detected in others,[36] including the present case. Bromides had been taken for a long period prior to the onset of symptoms in 3 cases [37] and after the onset in 1 case (Bailey,[8] fourth case), and iodides had been taken in 3 cases before symptoms appeared (Bailey,[8] second and third cases; Rosenberg and Cohen [16]) and in 2 cases after they began (Bailey,[8] fifth case; Shaffer [19]). No medication was taken prior to the onset of illness in other cases,[38] including the present one. With the exception of Bailey's [8] second patient, who improved when treatment with iodides was stopped and relapsed when it was started again, none of the patients seemed to be affected by such medication. Similarly, 4 of Bailey's patients had tonsillectomies or removal of diseased teeth without improvement. Whatever role active foci of infection or medication with bromides or iodides may play in the production of this syndrome, they cannot be considered to be major factors.

Differential Diagnosis.—Similar pathologic pictures with dissimilar clinical features can be produced by various agents. Localized atrophy of subcutaneous fat has occurred in persons with diabetes after the injection of insulin [39] and has been seen in narcotic addicts who used hypodermic injections. Trauma due to birth occasionally produces localized necrosis of subcutaneous fat.[40] Diffuse atrophy of subcutaneous fat without evidence of previous inflammatory changes (lipodystrophy [41]) usually involves the face and neck, but Bigler [42] has reported a case of diffuse, symmetric lipodystrophy involving only the lower extremities.

On the other hand certain diseases may simulate the Weber-Christian syndrome clinically but be entirely different pathologically. Biopsies have revealed various pathologic entities which in no way resemble nonsuppurative panniculitis. The subcutaneous fat nodules of adiposis dolorosa (Dercum's disease) may resemble the nodules of Weber-Christian disease, but those of the former remain unchanged for years. Erythema nodosum, erythema induratum and subcutaneous sarcoid of Darier and Roussy, as pointed out by Cummins and Lever,[1b] may resemble the initial lesions, but the nodules in these diseases do not progress to atrophy of the fat without change in the skin. Since dermatomyositis involves muscle as well as skin, there are severe pain on movement and considerable muscular weakness. The lesions of morphea, circumscribed scleroderma, are plaquelike, are slow to develop and regress and leave the skin shriveled and bound to the underlying tissues. Binkley [10] emphasized the differentiation of the Weber-Christian syndrome from malignant diseases of the breast. It is evident from these considerations that relapsing febrile nodular nonsuppurative panniculitis is a fairly distinct clinical entity but that it cannot be considered to be a pathologic entity.

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5 East Eighty-Fourth Street.
303 East Twentieth Street.

35. Cummins and Lever.[1b] Alderson and Way.[6] Brill.[7] Bailey.[8] Binkley.[10] Tilden, Gotshalk and Avakian.[11] Skiöld.[12] Hartwell and Thannhauser.[13] Rosenberg and Cohen.[16]

36. Gilchrist and Ketron.[1a] Hazel and Lamb.[1c] Pfeifer.[2] Weber.[3] Christian.[4] Netherton.[5]

37. (*a*) Weber.[3] (*b*) Rosenberg and Cohen.[16]

38. Gilchrist and Ketron.[1a] Cummins and Lever.[1b] Pfeifer.[2] Christian.[4] Netherton.[5] Alderson and Way.[6] Brill.[7] Bailey.[8]

39. (*a*) Rony, H. R.: "Lipo-Atrophy" in Obesity and Leanness, Philadelphia, Lea & Febiger, 1940, pp. 170-175. (*b*) Rowe, A. H., and Garrison, O. H.: Lipodystrophy: Atrophy and Tumefaction of Subcutaneous Tissue Due to Insulin Injections, J. A. M. A. **99**:16-18 (July 2) 1932. (*c*) Avery.[8]

40. (*a*) Shong, G., and Cowan, A.: Subcutaneous Fat Necrosis of the Newborn, Ohio State M. J. **31**:34-35 (Jan.) 1935. (*b*) Reed and Anderson.[9] (*c*) Tow, A.: Scleroderma (Adiponecrosis Subcutanea Neonatorum), in Diseases of the Newborn, New York, Oxford University Press, 1937, p. 436.

41. Parmelee, A. H.: Lipodystrophy, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Co., Inc., 1936, vol. 1, chap. 41, pp. 1-7.

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TRANSIENT PARALYSIS DUE TO BITE OF AMERICAN DOG TICK (DERMACENTOR VARIABILIS SAY)

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The paralysis caused by the bite of the female American dog tick, Dermacentor variabilis Say, is sufficiently rare to warrant reporting an additional case.

REPORT OF A CASE

F. J. S., a white girl 2 years and 10 months of age, was seen in St. Joseph's Hospital on Oct. 4, 1943, late in the afternoon. Her parents stated that her illness began with fever and restlessness late in the evening of the previous day. Approximately two hours later the child could not move in bed and asked her mother to help her. About five hours after the onset of the acute illness the mother discovered a distinct swelling of the posterior cervical glands on the left side and in a short time found an engorged tick in the scalp approximately 2 inches (5 cm.) from the hair line and a short distance posterior to the mastoid prominence. All attempts to dislodge the tick failed, and a physician was called. The physician arrived at approximately 8 a. m. on October 3 and removed the tick by means of a liquid. The tick was killed by the child's father and fortunately was saved. It was later identified by one of us (A. C.).

At the time the tick was dislodged the child's temperature was 101 F.; she was still unable to move her neck and remained in bed. Shortly after the tick was removed her temperature became normal, and in six hours the child got out of bed and felt like playing. At this time she began to move her neck, and the parents thought the child's condition was normal with the exception of a little soreness of the neck.

The past history of this child was essentially normal. She had been immunized against diphtheria and whooping cough. She had had no childhood diseases. There was a history of frequent sore throats. The child's temperature went up to a high level on October 3 in the late afternoon. On the following morning, her temperature was 105 F., and another physician was called. This physician was unable to account for the fever and suggested hospitalization.

When the child was seen in the hospital during a consultation of physicians on October 4 late in the afternoon, her temperature was 103.4 F. Her respiratory rate was 34, and her pulse rate was 110. She was lying quietly in bed and was fairly cooperative. The skin of the body was moist and warm and showed no abnormalities except on the left side of the scalp posteriorly. There in the area referred to by her parents was a small cutaneous lesion, 4 by 4 mm., containing a number of small intensely red areas, from a few of which some serum was oozing. The glands in the posterior triangle of the neck on the same side were enlarged and tender. The remainder of the physical examination yielded essentially normal results. No neurologic signs were present, and the child at this time could move her neck easily and turned in bed at will. The mother, when closely questioned, stated that the child had no difficulty in moving her neck a few hours after removal of the tick.

The laboratory findings were as follows: hemoglobin content (Sahli), 72 per cent; red blood cells, 4,400,000, and white blood cells, 19,700, with 30 per cent lymphocytes and 70 per cent neutrophils. The Wassermann reaction of the blood was negative. The urine was essentially normal. The tick was brought to the hospital by the father and later identified by one of us (A. C.) as a female American dog tick (Dermacentor variabilis Say). A roentgen examination of the chest was reported to show appreciable bronchovascular mottling in the right lung.

On the child's admission, her temperature was 103.4 F., and the following morning it was 99 F. It rose again in the afternoon of October 5 to 102 F. and shortly thereafter dropped to 99.2 F. and then remained normal. Sulfathiazole powder was used locally, and sulfadiazine was given by mouth. The glands in the left posterior cervical triangle rapidly decreased in size, and the tenderness diminished. The child was discharged from the hospital on October 6 and was later seen in the office. At that time the lesion in the scalp was almost healed, and the parents stated that she was none the worse for her experience.

COMMENT

A review of the literature reveals a number of reports [1] of paralysis due to the wood tick, Dermacentor andersoni Stiles. The first case of tick paralysis due to the female American dog tick, Dermacentor variabilis Say, was reported by Robinow and Carroll [2] in Georgia in 1938. A second case was reported by Mulherin [3] and a third by Beach and Ravenel.[4] The present case is the fourth to be reported, the first in this section of the country.

Regendanz and Reichenow [5] suggested that the weakness of the muscles is due to a toxin

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1. (*a*) McCornack, P. D.: Paralysis in Children Due to the Bite of Wood Ticks, J. A. M. A. **77**:260 (July 23) 1921. (*b*) Barnett, E. J.: Wood Tick Paralysis in Children, J. A. M. A. **109**:846-848 (Sept. 11) 1937.

2. Robinow, M., and Carroll, T. B.: Tick Paralysis Due to the Bite of the American Dog Tick, J. A. M. A. **111**:1093-1094 (Sept. 17) 1938.

3. Mulherin, P. A.: J. Pediat. **16**:86-88 (Jan.) 1940.

4. Beach, M. W., and Ravenel, B. O.: Tick Paralysis in South Carolina, J. South Carolina M. A. **37**: 323-325 (Dec.) 1941.

5. Regendanz, P., and Reichenow, E.: Ueber Zeckengift und Zeckenparalyse, Arch. f. Schiffs- u. Tropen-Hyg. **35**:255-273 (May) 1931.

produced in the developing ova of the impregnated female tick.

The present case is unique in that apparently there was a secondary infection that caused enlargement of the cervical glands and elevation of temperature. The patient was probably fortunate that this secondary infection occurred, for it was instrumental in the parents' finding the tick at an early stage of the child's illness.

The present case is also interesting for the reason that, like Mulherin's,[8] it occurred at the end of an epidemic of infantile paralysis.

SUMMARY

1. The case reported is the fourth recorded instance of paralysis caused by the female American dog tick, Dermacentor variabilis Say. The transient nature of the paralysis was probably due to the existence of a secondary infection, in the treatment of which the presence of the tick was disclosed, so that its removal was effected early. The paralysis occurred at the end of an epidemic of poliomyelitis and had to be differentiated from that infection.

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MYCOTIC ENDOCARDITIS

REPORT OF A CASE WITH NECROPSY; REVIEW OF THE LITERATURE

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Primary infection of the endocardium with higher organisms is uncommon. Because of the rarity of this type of infection and the difficulty in establishing the diagnosis, it has seemed worth while to report a case of this disease. This appeared especially desirable since the infection was controlled over a considerable period with sulfonamide compounds, an experience contrary to expectation with mycotic infections. Further, since the isolated cases of mycotic endocarditis reported in the literature had not been previously collected it seemed profitable in connection with a report of a case to make such a collection.

REPORT OF CASE

A. M., a 14 year old American boy born June 16, 1925, was admitted to the pediatric service of the University of Chicago clinics on April 25, 1940 with the complaint of chills and fever of two weeks' duration. The family history was not contributory; his father, mother and one brother were living and well. One sister had died at the age of 3 weeks. There was no history of rheumatic fever or heart disease in the family. The patient's birth had been normal, and he had grown and developed normally. He had whooping cough at 3 or 4 years of age, chickenpox at 4 and measles at 5. He was subject to frequent colds and had had pneumonia eight years previously. He had received no immunizations. Tonsillectomy and adenoidectomy had been done when he was 2 years of age.

In early December 1939, about five months before admission, he had complained of a cold, with fever, weakness and malaise. The morning after a day of considerable activity he had chills and fever, and these continued during the next two weeks, his temperature being 98 to 104 F. daily. During this period he was seen by a physician, who noted a systolic apical murmur at the first examination. He was hospitalized in his local hospital from Dec. 22, 1939 to Feb. 17, 1940, where it was evident that he had leukocytosis, anemia, which improved with transfusions of blood, hematuria and albuminuria. The diagnosis was bacterial endocarditis, and he received 0.6 Gm. of sulfanilamide four times a day from Dec. 22, 1939 to April 25, 1940. He continued to rest in bed, receiving weekly transfusions, until admission to the University of Chicago clinics.

Physical examination revealed a tall, thin boy, appearing chronically ill. The skin was pale and moist, without cyanosis but with a number of pinhead-sized petechiae scattered over the body. The conjunctivas were pale and showed petechiae; a small petechia with hemorrhage was seen in the right fundus. On May 1, 1940 a new hemorrhage was observed along the superior temporal vessels. The nose showed evidence of recent epistaxis. The buccal mucosa was pale, without petechiae and the tonsils were absent. The lungs were clear and resonant throughout. The heart rate was 110 per minute; the blood pressure was 128 systolic and 90 diastolic. There was no apparent cardiac enlargement. A loud, harsh systolic murmur was heard throughout the precordium and in the left axillary region; this was loudest at the apical area. In addition, on May 14, 1940 a faint, early diastolic murmur was heard at the apex. The abdomen was scaphoid; the edge of the liver was at the right costal margin, and the spleen could be palpated 3 cm. below the left costal margin. The notch was palpable. The extremities were thin, with considerable atrophy of the muscles. The toes were questionably clubbed; a petechia was present under the left great toe nail.

The laboratory findings and the clinical course from the patient's first admission on April 25, 1940, to the final admission, on March 31, 1942, will be considered together. Of

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considerable interest was the change in the clinical findings induced by variations in the treatment with sulfonamide compounds.

Blood Cultures.—Four cultures at another laboratory had shown no growth, with incubation varying from eighteen hours to seven days. Examinations of blood in our laboratory gave the following results:

Date Blood Taken for Culture	Time of Incubation in Hours	Organism
April 24, 1940	144	Gram-positive bacillus, probably contaminant
	168	Diphtheroids, probably contaminant
April 29, 1940	408	No growth
	432	Gram-positive coccus, contaminant
April 30, 1940	...	Nonhemolytic Staphylococcus albus
	576	No growth
May 8, 1940	...	Anaerobic culture—no growth
June 14, 1940	336	Anaerobic culture—no growth
June 28, 1940	336	No growth
July 24, 1940	328	No growth
Aug. 20, 1941	120	No growth
Aug. 20, 1941	120	No growth, despite use of paraaminobenzoic acid

Urine.—When the patient was admitted to the hospital the specific gravity of the urine was 1.015; it gave a 1 plus reaction for albumin; there was no evidence of sugar; the sediment contained 5 to 14 white blood cells and 38 to 78 red blood cells per high power field, centrifuged. Subsequently albumin was present in all specimens, the reaction usually being 1 to 2 plus, and the red blood cell count varied from gross blood to a few red blood cells.

Blood.—The blood contained 12,000 white cells, of which 69 per cent were polymorphonuclears, 24 per cent lymphocytes and 7 per cent monocytes. The hemoglobin content was 63 per cent, and the red cell count was 2,810,000. Subsequently the white cell count varied from 3,000 to 9,000, and the hemoglobin content and the red cell count varied; a severe anemia was usually present, partially controlled by frequent transfusions.

The nonprotein nitrogen content was 29.2 and 30.0 mg. per hundred cubic centimeters of blood on April 30, 1940 and May 11, respectively.

Electrocardiograms.—On April 27, 1940 the heart rate was 115. The PR interval was 0.35 second and the QRS interval 0.08 second. The T wave was low. There was no deviation of the axis. Subsequent tracings showed little change, but the final tracing, made on April 1, 1942, showed evidence of increasing myocardial damage.

Roentgen Examination.—On April 26, 1940 the heart was within the normal limit of size, but an irregular area of increased density was present at the superior pole of the left hilus, and a similar lesion was seen opposite the middle of the left hilus. On December 21 little change was noted except that the heart was slightly larger.

Course and Therapy.—After the patient's admission, before sulfonamide therapy was begun, the temperature reached 39.5 C. (103.1 F.) daily. On May 1, 1940 the administration of 0.62 Gm. of sulfapyridine every four hours was started, but, this drug being poorly tolerated, its use was discontinued on May 3. On May 14 sulfathiazole therapy was started, and this drug was given nearly continuously until March 10, 1942, three weeks before the final admission. The dosage until Jan. 1, 1941 was 0.5 Gm. every four hours, and from that date to Jan. 2, 1942, 1 Gm. every four hours. This amount was reduced to 5 Gm. daily from Jan. 3, 1942 to March 10. With these doses levels of the drug in the blood varied from 2.6 to 7.2 mg. per hundred cubic centimeters except when the drug was omitted entirely for a few days, either because the home supply was temporarily exhausted or because blood was to be taken for culture.

There was at once an excellent response to sulfathiazole therapy. The temperature remained nearly normal when the drug was given; the appetite improved, the petechiae disappeared and there was subjective improvement to the extent that the patient returned to school and was able to undertake limited activity. During the brief intervals when sulfathiazole was not taken, the temperature became elevated, petechiae appeared, hematuria increased and anorexia recurred. This observation was confirmed by several persons and was noted by the family. It was apparent that, while medication readily depressed the signs of active infection, the infection persisted and became evident clinically when use of sulfathiazole was discontinued for a few days. However, the systolic murmur persisted and

became louder, and the apical diastolic murmur was more easily heard. The spleen remained large; the edge of the liver remained at the right costal border. Occasional transfusions were given for the persistent anemia.

On Jan. 3, 1942, after discharge from the hospital, where he had been for two days for transfusions, the patient did not feel as well as previously, becoming progressively weak and tired. During the next two months he had grossly bloody urine, but the urine was clear for three to four weeks before his final admission. His family reported that he had no fever during this time and that they had noticed no petechiae until March 31, 1942, the date of his final admission to the hospital. Edema of the ankles was noticed three days prior to this

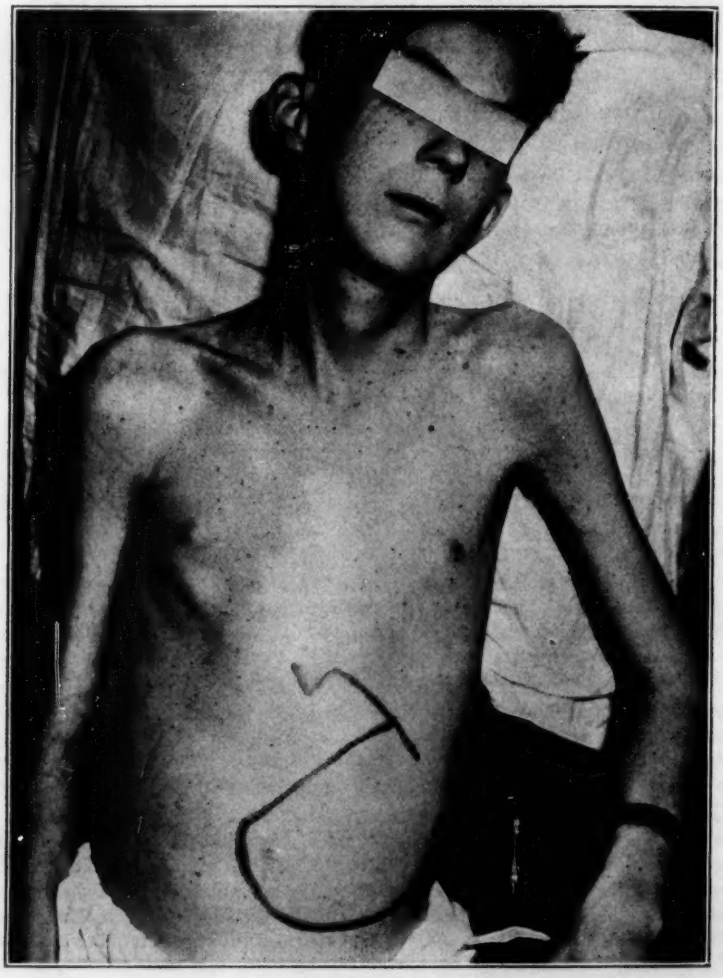

Fig. 1.—Photograph showing the numerous petechiae.

hospitalization. He continued to take 5 Gm. of sulfathiazole daily until about March 10, 1942, three weeks previous to hospitalization, when its use was discontinued without medical consultation.

He was now 16 years and 9 months of age and was therefore admitted to the medical service at the University of Chicago clinics on March 31, 1942.

Physical examination showed a pale, cachectic adolescent boy. There were numerous petechiae on both eyelids and on the conjunctivas of both lower lids, where they showed white centers. The fundi showed no papilledema. In the superior nasal field of the right fundus was a red oval area with a yellow-white center. There were scattered bright red petechiae on the pharyngeal mucosa. The lungs were resonant, with occasional rales at the

bases. The heart was grossly enlarged, with the point of maximal impulse and left border dulness 13 cm. and the midclavicular line 8 cm. from the midsternal line. The sounds were regular and loud; the systolic blood pressure was 100 mm. of mercury and the diastolic 50. The loud systolic apical murmur was transmitted to the axilla and back, and upward along the left sternal border to the base of the heart. A soft presystolic apical murmur was present. The second pulmonic sound was loud. There was a large, hard mass filling the left upper quadrant of the abdomen, extending inferiorly 2 to 3 fingerbreadths below the umbilicus and medially past the midline. The edge of the liver was at the right costal margin. Rectal examination revealed a small, slightly tender fluctuant mass just above the prostate. There were no abnormal neurologic signs.

Laboratory Examinations.—Five examinations of the urine showed a specific gravity of 1.017 to 1.020, a trace of albumin to a 4 plus reaction, occasional granular and cellular casts and white blood cells, and up to 100 red blood cells per high power field. A blood count showed 3,100 white cells with 71 per cent polymorphonuclears, 24 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils; the concentration of hemoglobin was 4.5 Gm. per hundred cubic centimeters of blood, and there were 2,060,000 red cells. The anemia improved after several transfusions. On April 8, 1942 a congo red test showed that 88 per cent of the dye was left in the blood (a normal result). On April 8 the blood contained 4.26 Gm. of plasma protein per hundred cubic centimeters, 2.23 Gm. of albumin and 1.93 Gm. of globulin. The albumin-globulin ratio was 1.2. The nonprotein nitrogen content was 76.0 mg. per hundred cubic centimeters of blood. On April 10 the urea clearance was 14 according to the square root formula. The urea nitrogen content of the blood was 47.1 mg. per hundred cubic centimeters. On March 31 a roentgen examination showed that the heart was grossly enlarged, with early congestive changes present at the right hilus.

Blood cultures taken March 31 and April 3 showed gram-negative pleomorphic filamentous rods in tangled masses in the broth culture; those taken March 31 and April 7 showed a few colonies of an organism with similar staining and morphologic characteristics. Subcultures did not grow, and consequently positive identification of the organism was not possible.

The patient's temperature rose daily to 39 C. (102.2 F.) for seven days and then remained at a somewhat lower level. Many petechiae appeared on the face. When the blood culture revealed a fungus, potassium iodide was given for three days, and on the second day an extensive crop of petechiae appeared over the trunk and the arms and in greatest numbers around the eyes. They were 0.5 mm. to 2 mm. in diameter and purple-red. On April 15, 1942 the blood pressure was 80 systolic and 60 diastolic, and deep somnolence was present. Four grams of sulfadiazine was given, but death occurred on April 16.

NECROPSY

The body was that of a slender, emaciated white boy 67 inches long, weighing 107 pounds (48.5 Kg.). The skin showed hundreds of petechial hemorrhages up to 4 mm. in diameter, varying from red through brown to tan. There was a slight edema of the feet, legs, scrotum and back of the trunk.

Body Cavities.—The peritoneal cavity contained 1,100 cc. of pale amber, slightly cloudy fluid. The surfaces were everywhere more opaque and thicker than normal, and they were uniformly studded with petechial hemorrhages 2 to 3 mm. in diameter, which varied in color from red through purple to tan. The right pleural cavity contained 780 cc. and the left 220 cc. of fluid resembling that found in the abdomen. There were edematous fibrous adhesions on the posterior surfaces of both lungs. The pericardial sac contained 220 cc. of fluid similar to that found in the other serous cavities.

Heart and Blood Vessels.—The emptied heart weighed 355 Gm. The configuration was altered a little because of a slight dilatation of each ventricle. The myocardium was flabby and was pale reddish brown mottled by numerous petechial hemorrhages. It measured 3 to 4 mm. in the right ventricle and from 4 to 11 mm. in the left ventricle. Measurements of the heart valves were as follows: tricuspid, 11.5 cm.; mitral, 11.0 cm.; pulmonic, 7.8 cm., and aortic, 7.2 cm. The tricuspid and pulmonic valves appeared normal. The mitral valve showed almost a continuous row of vegetations on both cusps, centering at approximately the line of closure but extending down on the chordae tendineae and up on the surfaces of the valve (fig. 2 *C*). They were rough and warty and were mottled yellow and red. The largest vegetation measured 26 by 16 by 5 mm. They were friable but firmly adherent. Except for the massive vegetations the mitral valve showed little recognizable abnormality. The aortic valve showed a single vegetation attached in the commissure between the anterior and the right posterior cusp. It measured 12 by 8 by 7 mm. (fig. 2 *B*). The valve other-

wise appeared normal. This mural endocardium was mottled by innumerable petechial hemorrhages. Under the epicardium of the anterior surface of the left ventricle was an elevated soft, fluctuant nodule, 9 by 7 mm., which on incision exuded a creamy, yellow pus (fig. 2 *A*). A similar nodule 3 mm in diameter was found on the posterior surface of the left ventricle. Both of these abscesses were situated in the course of visible blood vessels.

In the course of a small artery at the hilus of the left kidney was a bulbous, firm swelling 9 mm. in diameter. It was filled by a laminated thrombus. In the distal end of the left hypogastric artery and its main branches in the lateral pelvic wall was an oval

Fig. 2.—*A*, photograph of the heart, showing an abscess and numerous petechiae. *B*, photograph to show the size and extent of the vegetations on the aortic valve. *C*, photograph to show the extensive vegetations on the mitral valve. *D*, photograph of the left hypogastric artery with an aneurysm in its course.

mass 7 by 5.5 by 4.3 cm., weighing 105 Gm. It protruded into the pelvic cavity, elevating the peritoneum, and was firm. It had a thin (1 to 2 mm.) fibrous capsule and was filled by a laminated, firm thrombotic mass varying from white to red (fig. 2 *D*).

Respiratory Tract.—The mucosa of the trachea and the bronchi was studded with petechial hemorrhages. Each lung weighed about 500 Gm. The lungs were small, subcrepitant and reddish purple. The cut surfaces showed a uniform bloody edema. In addition, histologic examination disclosed a moderately advanced chronic passive congestion.

Alimentary Tract.—The mucous membrane of the mouth and the pharynx showed petechial hemorrhages, while that of the esophagus showed a solitary linear erosion. The gastric mucosa also showed numerous petechial hemorrhages. The walls of the intestines were thickened by edema, and both the mucosa and the serosa showed petechial hemorrhages. There were several miliary abscesses in the submucosa.

Liver and Biliary System.—The liver weighed 2,450 Gm. It showed a mottled surface and large hepatic lobules, which had dark centers and wide, pale peripheral zones. Microscopically the picture was that of passive congestion and of many periportal hemosiderophages. The wall of the gallbladder was edematous, measuring 4 mm.

Spleen.—The spleen weighed 1,720 Gm. The normal configuration was retained. Externally it showed numerous depressed, scarred areas resembling old infarcts and one elevated hemorrhagic infarct. The pulp was purplish red, with large malpighian bodies. Beneath the depressed areas were infarcts with yellow centers. From one of these a thick, pale yellow pus exuded. Microscopically the splenic enlargement was due to engorgement, reticulum cell hyperplasia and a little fibrosis.

Urinary Tract.—The right kidney weighed 155 Gm. It showed a large scar, two infarcts, each 1 cm. in diameter, and numerous punctate hemorrhages throughout the cortex. The renal pelvis showed many petechial hemorrhages. The left kidney weighed 130 Gm. It had no scar and only one recent infarct; in other respects it resembled the right. In addition, its pelvis was dilated, as was its ureter down to a point where it passed over the left pelvic aneurysm; there it was compressed to a ribbon-like structure but was not anatomically obstructed. The mucosa of the bladder showed a few petechial hemorrhages.

A microscopic examination of the kidneys showed an advanced stage of chronic and acute glomerulonephritis in addition to the healed and the recently formed infarcts. Many glomeruli and tubules were the sites of tiny areas of suppuration.

Lymph Nodes.—Throughout the body the lymph nodes were enlarged, soft and pale pinkish brown. Beneath the bifurcation of the trachea the mass of lymph nodes had a maximum diameter of 5.5 cm., while the periportal and mesenteric nodes measured up to 3.0 cm. A microscopic study of the nodes showed simple hyperplasia and many hemosiderophages.

Other Structures.—The thymus appeared involuted. The thyroid, the parathyroids, the pancreas, the adrenals, the generative organs, the muscles and the skeleton were not remarkable. The brain was not examined. The bone marrow was hyperplastic and showed numerous hemosiderophages.

Microscopic Examination.—In addition to the microscopic observations already mentioned, the most interesting changes were seen in the heart, the abscesses, the infarcts and the aneurysms.

The myocardium showed minute fibrous scars and minute foci of myocarditis. The epicardial abscesses showed a fibrous capsule and a center consisting of fluid, fibrin, polymorphonuclear leukocytes and colonies of organisms resembling those seen on the valves of the heart (fig. 3*A*). The vegetations on the aortic and mitral valves consisted mainly of fibrin, which was relatively cell poor and which showed areas of liquefaction. The bases of these vegetations showed a certain amount of fibrous organization, and here the leukocytic reaction was intense. The inflammatory reaction extended to the mural endocardium adjacent to the valves.

Great colonies of micro-organisms were found scattered throughout the vegetation, but they were especially numerous on or near the surfaces, where they formed almost continuous sheets (fig. 3*B*). The organisms took two forms, namely, slender, long filamentous branching rods (fig. 3*C*) and small round or oval bodies. Usually both forms were found together, although the filamentous forms existed alone as matted masses and the round bodies also formed large colonies. Where they coexisted the filamentous forms protruded from the margins of the colony (fig. 3*C*). Both forms of the organism were gram-negative and non-acid-fast. The centers of many of the larger colonies showed liquefactive degeneration. To many colonies there was no leukocytic reaction whatever.

Colonies of micro-organisms resembling those described on the cardiac valves were also seen in the myocardial and epicardial abscesses, in a septic splenic infarct, in small renal foci of suppuration located in glomeruli and in tubules, and in the intestine. They were not found in the bland renal and splenic infarcts or in the renal and pelvic aneurysms, where no prolonged search was made for them.

The final anatomic diagnoses were as follows: subacute, thrombotic, mycotic endocarditis involving the mitral and aortic valves; recent and ancient infarcts in the spleen and the kidneys; embolic glomerulonephritis; petechial hemorrhages in the skin and in many mucous and serous membranes; abscesses in the heart, the spleen, the intestine and the kidneys; aneurysms

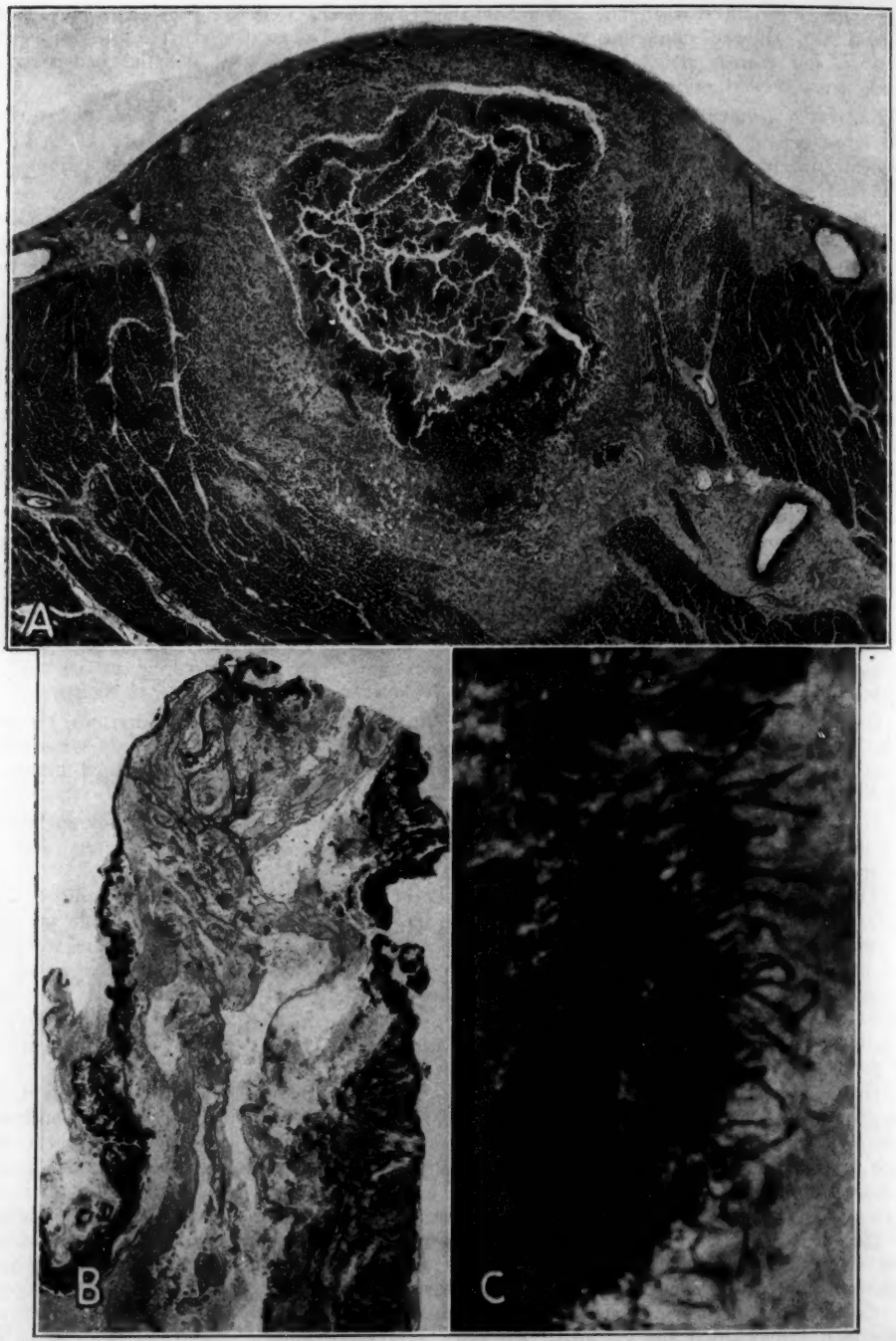

Fig. 3.—*A*, photomicrograph (× 13.5) showing an abscess in the heart. In the abscess are three colonies of the organism (toluidine blue–phloxine stain). *B*, photomicrograph (× 13.5) of a vegetation on the mitral valve. The dark border is composed of masses of the micro-organisms. There is practically no reaction here (toluidine blue–eosin stain). *C*, photomicrograph (× 1,900) showing the micro-organisms on the margin of the vegetation of *B*. The filamentous forms project from the surface. In the vegetation are round, granular bodies (toluidine blue–phloxine stain).

(mycotic?) in the hypogastric and renal arteries; severe anemia; generalized passive congestion; ascites; bilateral hydrothorax and hydropericardium; anasarca; bilateral chronic pulmonary congestion; bilateral focal fibrous pleuritis; marked splenomegaly; generalized hyperplasia of lymph nodes.

COMMENT

In summary, a 14 year old school boy became ill in December 1939 and showed the signs and symptoms of subcute bacterial endocarditis until his death, on June 16, 1942. The laboratory findings, with the exception of negative blood cultures, were compatible with this diagnosis. In spite of repeated cultures obtained under various conditions the offending organism could not be isolated until the patient's final hospitalization. It should be emphasized that the positive cultures were obtained after administration of a drug had been omitted for three weeks. This was the longest interval during which sulfonamide compounds had not been given to the patient. This fact, when added to the clinical evidence that the infection could be controlled by sulfathiazole, seems to indicate that the mycotic infection responded to but was not cured by this treatment. The duration of the illness, about two years and four months, appears to be further evidence that this therapy was useful in treatment.

While the organism could not be specifically identified, the structure of the growth on culture and in microscopic sections appeared the same, and we believe that this indicates that the condition was a primary mycotic infection of the endocardium, which was clinically indistinguishable from subacute bacterial endocarditis due to a bacterium. There is no evidence that the fungous infection was superimposed on a previous bacterial infection.

REVIEW OF THE LITERATURE

Few cases of mycotic endocarditis have been reported in the literature. Jervell [1] in 1922 reported the case of a 20 year old man who had severe rheumatic fever at the age of 12 years. He had chills and fever and showed evidence of heart disease. Cultures of the blood revealed an organism identified as Leptothrix, and the same organism was cultured from the spleen and valves of the heart at autopsy. Wagner, Maiorov and Steriopoulo [2] in 1927 reported the case of a 44 year old man who was admitted to the hospital with cardiac decompensation. His heart was enlarged, and a loud systolic murmur was present. The liver and the spleen were enlarged. An organism identified as Streptothrix was cultured during life from the blood. On autopsy endocarditis of the mitral and aortic valves was present, and the organism was found in material taken from the valves.

In 1937, Alestra and Girolami [3] reported 2 cases which they believed were instances of endocarditis due to Nocardia. The patient in their first case was an 18 year old youth who had fever and malaise. Examination showed cardiac enlargement, and apical systolic murmur and splenomegaly. The organism obtained by blood culture was reported to have the characteristics of Nocardia. An iodide was administered intravenously, and the temperature gradually fell to normal, the splenomegaly disappearing. The cardiac signs persisted during the subsequent two years he was followed. He was not seen after this, and the final outcome was not known. In their second case the patient was a 37 year old woman who had

1. Jervell, O.: Leptothrix in the Blood in a Case of Endocarditis, Norsk mag. f. lægevidensk. **83**:36 (Jan.) 1922.

2. Wagner, G.; Maiorov, G., and Steriopoulo, S.: Infectious Endocarditis Caused by Streptothrix and Its Mutants: Case, Russk. Klin. **8**:315-324 (Sept.) 1927.

3. Alestra, L., and Girolami, M.: Endocarditis Caused by Nocardia: Two Cases, Policlinico (sez. med.) **44**:441-463 (Sept.) 1937.

malaise, anorexia, chills and fever. This condition had been diagnosed as congenital heart disease when the patient was 11 years of age. Examination revealed cardiac enlargement, and a systolic thrill and murmur were most intense at the midsternum. The spleen and the liver were enlarged. The organism obtained on blood culture was studied in detail and was described as a mycete of the family Nocardiaceae. Autopsy revealed a defect in the membranous part of the interventricular septum and a polyp-like endocarditis of the pulmonary valve and the conus of the pulmonary artery.

Friedman and Donaldson [4] reported the observations at autopsy on a 57 year old man in whose case the clinical diagnosis of subacute bacterial endocarditis had not been confirmed by blood culture. Postmortem examination showed a luxuriant vegetation on the aortic valve, and nests of yeastlike cells were seen on the microscopic sections. The organism was not further identified.

Uhr [5] reported the case of a 24 year old man who had malaise, nausea, vomiting and a high temperature. The heart was not enlarged on examination, but a soft systolic murmur was heard, localized at the apex. Petechiae appeared over the body, and later large purpuric areas. Each of four consecutive cultures of the blood yielded a pure growth of Actinomyces bovis. The organism required four to eight days for growth, grew only in the presence of blood and required reduced tension of oxygen for isolation. Autopsy showed a large friable vegetation on the mitral valve and a small vegetative lesion on the endocardium of the left auricle, similar to the valvular lesion. Culture of the mitral vegetation showed A. bovis. Uhr reviewed the literature regarding actinomycotic infection of the heart; he pointed out that the cases reported previous to his were not instances of primary endocardial infection but cases of direct extension or metastatic spread.

Russell and Lamb [6] reported a case in which a 37 year old man entered the hospital complaining of continuous pain in the right leg of four days' duration. There had been progressive weakness, malaise and loss of weight for two months previously. Examination revealed cardiac enlargement, a systolic thrill in the aortic area, a precordial systolic murmur loudest at the base and transmitted into the neck and a long, blowing diastolic murmur at the apex. The right foot and the lower third of the tibia were cold and blanched. Six blood cultures showed a small, slender, straight or slightly curved gram-positive bacillus, identified as Erysipelothrix rhusiopathiae. At autopsy the anatomic diagnoses were subacute bacterial endocarditis of the aortic and mitral valves with mycotic aneurysm and abscess formation, bicuspid aortic valve, infarct of spleen, fibrinous pericarditis and hydrothorax. The organism obtained by blood culture was studied in detail, and the authors presented a discussion of infection in swine and man due to this organism, with a review of the literature. While the authors found reports of 3 probable cases of endocarditis due to this organism in the literature, in 2 cases bacteriologic confirmation was lacking and in the third case the organism was found in blood cultures but a necropsy was not done. Further details of these cases and references to the literature dealing with infection with Erysipelothrix rhusiopathiae will be found in this excellent paper.

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4. Friedman, N. B., and Donaldson, L.: Systemic Mycosis with Mycotic Endocarditis, Arch. Path. **27**:394 (Feb.) 1939.

5. Uhr, N.: Bacterial Endocarditis: Report of a Case in Which the Cause Was Actinomyces Bovis, Arch. Int. Med. **64**:84-90 (July) 1939.

6. Russell, W. O., and Lamb, M. E.: Erysipelothrix Endocarditis: A Complication of Erysipeloid, J. A. M. A. **114**:1045-1050 (March 23) 1940.

Three cases of mycotic endocarditis due to Monilia have been reported. Joachim and Polayes [7] first reported monilia endocarditis in a 48 year old man who was addicted to the use of drugs. He was admitted to the hospital because of abdominal pain of two days' duration. For about three months he had not taken drugs and had lost weight and had become weaker. Fever had developed. Physical examination revealed fever, cachexia and a loud, rough aortic systolic murmur. The liver and the spleen were enlarged. Petechiae appeared, and tender nodules developed on the soles. Each of eleven blood cultures showed many colonies of yeastlike cells. The organism was later identified as Candida (Monilia) parakrusei.[8] Autopsy showed monilia endocarditis and fibrosis and calcification of the aortic valve; direct smear of vegetations of the aortic valve showed budding fungi. Culture of these showed Monilia, Streptococcus nonhaemolyticus and Bacillus coli.

Wikler, Williams, Douglass, Emmons and Dunn [9] reported a case in which the patient was a 49 year old man, also addicted to the use of drugs. Admission to the hospital had been for treatment for this habit and physical examination at that time gave essentially negative results. The serologic reaction of the blood was positive, however, and antisyphilitic therapy was begun. After he had been in the hospital for about four months, mental confusion and signs of a right hemiplegia suddenly developed. The spleen was found to be enlarged; a loud systolic apical murmur transmitted to the axilla was present, and he became febrile. Blood cultures on two occasions showed a yeastlike growth later identified as Candida (Monilia) parakrusei. Autopsy showed a large vegetative growth attached to the mitral valve, and microscopic examination showed that clumps of spores were present in the exudate over the surface of the valve.

In addition to the case reported by Joachim and Polayes and their own case, the authors referred to 3 other cases of mycotic endocarditis in drug addicts. Details of these cases are not available at this time.

Pasternack [10] reported a case in which a 45 year old man was admitted to the hospital with complaints of epigastric pain, fever, anorexia, thirst and nausea of two weeks' duration. Examination showed cardiac enlargement, a palpable thrill and a loud systolic murmur at the aortic area and a blowing systolic murmur at the apex. The liver was enlarged and became larger; petechiae appeared. The spleen was not palpable. Six blood cultures all showed budding yeastlike cells, singly and in clusters. Autopsy showed a gray vegetation arising from the region of the aortic valve and a hard reddish tumor mass bulging into the right antrum and protruding into the ring of the tricuspid valve. Sections showed nests of yeastlike cells in the vegetations. The morphologic and cultural characteristics of the organism were considered compatible with those of Candida (Monilia) parakrusei.

SUMMARY AND CONCLUSIONS

Ten cases of mycotic endocarditis reported in the literature have been briefly reviewed. Adequate confirmation of the diagnosis in the first case of Alestra and Girolami [3] is lacking, and perhaps it should not be included. Likewise, the report

7. Joachim, H., and Polayes, S. H.: Subacute Endocarditis and Systemic Mycosis (Monilia), J. A. M. A. **115**:205-208 (July 20) 1940.

8. Polayes, S. H., and Emmons, C. W.: Final Report on the Identification of the Organism of the Previously Reported Case of Subacute Endocarditis and Systemic Mycosis (Monilia), J. A. M. A. **117**:1533-1534 (Nov. 1) 1941.

9. Wikler, A.; Williams, E. G.; Douglass, E. D.; Emmons, C. W., and Dunn, R. C.: Mycotic Endocarditis: Report of a Case, J. A. M. A. **119**:333-336 (May 23) 1942.

10. Pasternack, J. G.: Subacute Monilia Endocarditis, Am. J. Clin. Path. **12**:496-505 (Sept.) 1942.

of the case of Friedman and Donaldson [4] is incomplete. If these are acceptable, then the 3 cases of Erysipelothrix infection referred to by Russell and Lamb [6] probably should be included in the list of cases of mycotic endocarditis. If the incomplete cases are included, 13 cases of mycotic endocarditis have been reported. To these we have added a case in which the diagnosis was confirmed by culture and by autopsy. However, the organism was not specifically identified, because of its failure to grow in the subcultures.

Studies of a sufficient number of cases of mycotic endocarditis are available to indicate that this condition represents a subdivision of the general category of subacute bacterial endocarditis. Frequently, as in bacterial endocarditis, valvular lesions from other infections are present previous to the onset of the endocardial infection. The clinical course appears to be indistinguishable from that of subacute bacterial endocarditis, and the laboratory findings, with the exception of blood cultures, are similar. In cases where the clinical findings suggest the diagnosis of subacute bacterial endocarditis, it is obvious that unusual organisms present in blood cultures should not be casually dismissed as contaminants, especially if these are present in repeated cultures. Likewise, negative blood cultures suggest the use of special mediums and especially long periods of incubation.

As interest in mycotic infection in man increases, it seems likely that mycotic endocarditis will be found to be more common than a survey of the literature indicates and that the variety of organisms responsible for the infection will be found to be diverse.

The case reported by us raises the question whether adequate treatment with sulfonamide compounds may not be of value in treatment in some instances of mycotic infection.

This case is reported by permission of Dr. Wright Adams.
The blood cultures were reported by Miss H. Van Sant.

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Progress in Pediatrics

RECURRENT AND CHRONIC DIARRHEA IN INFANCY AND CHILDHOOD

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The multiplicity of theories regarding the causes of recurrent and chronic diarrhea in infancy and childhood reflected the poor understanding of the subject until Andersen,[1] by differentiation of cystic fibrosis of the pancreas from the other syndromes given the name of celiac disease, stimulated attempts at reclassification.

While there is still no unanimity of opinion as to the relationships of these syndromes, sufficient facts are now available to justify an attempt at classification. In the outline which follows I have in the main adopted Andersen's classification, and I shall discuss each of the groups listed below and describe cases illustrative of each type of metabolic diarrhea.

CLASSIFICATION

1. Diarrhea due to overfeeding and grossly improper feeding.
2. Parenteral diarrhea, due to gastrointestinal manifestations of systemic infections.
3. Infectious and toxic diarrhea and the vague gastrointestinal intoxications.
4. Mechanical diarrhea.
5. "Metabolic" diarrhea, the celiac syndrome.
   - (*a*) Cystic fibrosis of the pancreas—onset at birth.
   - (*b*) Intolerance to starch—onset at the age of 3 to 12 months.
   - (*c*) Infantile steatorrhea—onset at the age of 1 to 8 months.
   - (*d*) "Celiac disease," steatorrhea—onset at the age of 10 to 60 months.
   - (*e*) "Allergic celiac" syndrome.

The study of recurrent and chronic diarrhea in infancy and childhood is beset with many difficulties, since diarrhea is so common a symptom in this age group. Generally speaking, diarrhea due to overfeeding or to grossly improper feeding is easily recognized by the history, the explosive onset and the rapid response to any of the usual procedures adapted to the case, such as underfeeding, administration of pectin agar or of scraped apple and parenteral therapy. Diarrhea of parenteral origin, a gastrointestinal manifestation of a systemic infection such as acute follicular tonsillitis, pneumonia or otitis, is almost invariably febrile and explosive in onset and subsides rapidly with the cure of the causative disease. In some cases of metabolic diarrhea, especially of the type caused by intolerance to starch, otitis is not uncommon, and differentiation is difficult.

Diarrhea due to infective agents falls into fairly well recognized classes, such as epidemic diarrhea of the newborn, amebic dysentery, salmonella infections, the food poisoning enteritides and toxemia due to infection with staphylococci. Usually, careful bacteriologic studies of the stools early in the course of the disease, together with serum agglutination tests at a later stage, are sufficient to differentiate diarrhea of this type from that of the metabolic type. Occasionally recurrent or chronic diarrhea in a patient of this age group may prove to be the subacute or chronic sequel to an attack of acute, infectious diarrhea, but usually the infectious nature of such diarrhea can be detected by the history of pus or blood in the stool, explosive onset and rapid response to therapy with sulfonamide compounds.[2] It is only rarely that bacteriologic studies of the stool, serum agglutination tests and proctologic examinations fail to disclose the etiologic agent in infectious diarrhea. Epidemic diarrhea of the newborn[3] and the so-called

1. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease, Am. J. Dis. Child. **56**:344 (Aug.) 1938; Pancreatic Enzymes in the Duodenal Juice in the Celiac Syndrome, ibid. **63**:643 (April) 1942. Andersen, D. H., and Hodges, R. G.: Celiac Syndrome and Cystic Fibrosis of the Pancreas, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1942, vol. 1, chap. 29.

2. (*a*) Halpern, S. R., and Cunningham, J.: Bacteriologic and Chemotherapeutic Studies in Acute Diarrhea of Infants and Children, J. Pediat. **21**:184 (Aug.) 1942. (*b*) Tudor, R. B.: The Chemotherapy of Infantile Diarrhea: A Comparison of Sulfathiazole and Sulfaguanidine, ibid. **20**:707 (June) 1942. (*c*) Taylor, G.: Sulfathiazol Therapy of Infantile Diarrhea, ibid. **18**:469 (April) 1941. (*d*) Cooper, M. L.; Zucker, R. L., and Wagoner, S.: Sulfathiazole for Acute Diarrhea and Dysentery of Infants and Children, J. A. M. A. **117**:150 (Nov. 1) 1941.

3. Felsen, J., and Wolarsky, W.: The Prevention and Treatment of Infectious Diarrhea of the Newborn with Lyophile Plasma and Sulfathiazole, Arch. Pediat. **58**:751 (Dec.) 1941.

intestinal influenza often occurring during epidemics of influenza in adults are both so acute in onset and so short in duration that no difficulty should present itself in the differential diagnosis. The vague gastrointestinal intoxications resulting so frequently in dehydration, acidosis and marasmus in young infants perhaps belong with infectious diarrhea. This category includes the more severe attacks or the low point in the course of several types of diarrhea (allergic and infectious diarrhea and the metabolic types associated with steatorrhea and intolerance to starch). Differentiation of infectious from "metabolic" diarrhea is not always possible, since associated infections may bring on celiac crises and bouts of acidosis and dehydration in patients with metabolic diarrhea too. However, the onset of gastrointestinal intoxication is usually more acute; roentgenographic examination of the chest and gastrointestinal tract usually reveals no abnormality, and the swift decline into dehydration and marasmus is more acute than is usual in cases of metabolic diarrhea.

Diarrhea due to mechanical causes results from mechanical disturbances in the absorption of fat from the intestine (*a*) by a short circuit of the intestine, such as occurs with gastrocolic fistula or intestinal malrotation, (*b*) by a specific lesion which alters the peristalsis, such as stenosis, or (*c*) by establishment of an actual barrier to the passage of fat through the intestinal wall, or mesenteric lymphadenitis, such as is produced by abdominal tuberculosis or by giardiasis. For this reason, infants successfully operated on for malrotation of the intestine or infants suffering from partial stenosis not severe enough for operation will frequently in later infancy present a picture similar to that seen in cases of metabolic diarrhea.

When the aforementioned types have been eliminated, one is confronted with a large group of cases in which either chronic diarrhea over months or frequent episodes of diarrhea have occurred and have been neglected. Mothers and even physicians are all too prone to be satisfied with the explanation that the "baby has diarrhea with every tooth," and many physicians are still inclined to restrict the use of the word diarrhea to frequent watery stools and to neglect to question mothers about the consistency, oiliness and daily volume of stools. Fanconi [4] and Morse [5] years ago noted the different types of stools found in chronic diarrheas, but quantitative examination of the stools and correlation of the types of stools with the different syndromes of chronic diarrhea were not attempted. Close questioning of the mothers and frequent gross examinations of the stools, together with chemical tests for fat and microscopic examinations for undigested starch whenever the diagnosis is questionable will bring to light numerous cases of "metabolic" diarrhea. This type of diarrhea is not necessarily persistent; it may be episodic, as in attacks precipitated by infections of the upper respiratory tract, by gross overfeeding with starch or by intolerance to starch. The stools are rarely watery; much more commonly they are mushy, of oatmeal consistency, foul smelling and bulky. They are often normal in texture though pale, and the increased bulk may not be apparent on examination of a single specimen. The important factor in arousing suspicion is the twenty-four hour volume of stool; repeated questioning often elicits the fact that the baby seems "to pass as much as he eats," far more than is usual.

REPORT OF CASES

A case will be described to illustrate each subdivision of the "metabolic" diarrhea given in the classification at the beginning of this article. For the sake of completeness, I am presenting, as an illustration of cystic fibrosis of the pancreas, a case reported by Flax, Barnes and Reichert.[6]

CASE 1.—*Cystic fibrosis of the liver.*

The patient was a full term baby who did not gain well though a number of different formulas were tried, who always had four to five large, greasy, foul-smelling stools a day and who repeatedly showed evidence of acute bronchitis. At 13 months of age, the child weighed 13 pounds 8 ounces (6.1 Kg.). The total content of cholesterol was 114 mg. per hundred cubic centimeters of blood, and roentgen examination of the chest showed "soft tissue accentuation of the dependent bronchi along both heart borders—peribronchial infiltration." A flat curve was obtained in a test of the absorption of vitamin A. The child did fairly well subsequently on a high protein diet plus pancreatin. In the meantime, a sister of this patient died, and an autopsy showed that she had cystic fibrosis of the pancreas.

While no study of pancreatic enzymes or examination of the lungs and pancreas could be made in this case, the combination of intestinal and respiratory symptoms, the low content of cholesterol in the blood, the flat curve of vitamin

4. (*a*) Fanconi, G.: Der intestinale Infantilismus und ähnliche Formen der chronischen Verdauungsstörung, Abhandl. a. d. Kinderh., 1928, no. 21. (*b*) Fanconi, G.: Uehlinger, E., and Knauer, C: Das Coeliakiesyndrom bei angeborener zystischer, Pankreasfibromatos und Bronchiektasien, Wien. med. Wchnschr. **86**:753 (July 4) 1936.

5. Morse, J. L.: Progress in Pediatrics: Celiac Disease, New England J. Med. **204**:668 (March 26) 1931.

6. Flax, L. J.; Barnes, M., and Reichert, J. L.: Vitamin A Absorption and Its Relation to Intestinal Motility in Fibrocystic Disease of the Pancreas, J. Pediat. **21**:475 (Oct.) 1942. Case reported by courtesy of Dr. J. L. Reichert.

A absorption and the existence of the disease in a sibling make the diagnosis of cystic fibrosis of the pancreas fairly plausible.

The differentiation of cystic fibrosis of the pancreas from the other types of celiac syndrome has been fully elaborated by Andersen [1] and other workers [7] and will not be repeated here. However, I wish to point out that analysis of the stools in these cases often gives the first clue. The daily weight of the stools will run from 100 to 1,000 Gm., over 85 per cent of which is water; undigested starch is present in normal form only and there is 30 to 80 per cent of fat in the dried stool. The difficult analyses for the products of the partial digestion of fats in all probability need not be made, inasmuch as the percentage of split fats is not a differential point. In 7 cases reported by Deem and McGeorge [7f] the total fat ranged from 39.4 to 57.0 per cent, the neutral fat from 2.3 to 42.3 per cent, soaps from 2.8 to 36.2 per cent and fatty acids from 2.5 to 26.0 per cent.

CASE 2.—*Diarrhea due to intolerance to starch.*

Diarrhea due to intolerance to starch may be exemplified by the case of D. G., who suffered from recurrent episodes of diarrhea beginning at 3 months of age. These episodes usually coincided with respiratory infections. When the child was 2 years of age, a diarrheal episode lasted four months in spite of the institution of a diet of protein milk, banana and pot cheese. Analysis of the stools at this time (by Dr. D. Andersen) showed total weight 155 Gm. per day (about 300 per cent of normal), water 88.05 per cent (compared with a normal content of less than 80 per cent), total fat 18.6 per cent of the dry weight (normal) or 3.4 Gm. (a little high). The excess of fat was due to the increased total bulk, as the percentage of fat was normal. Digestion of starch was not complete. These results are all to be expected in a case of intolerance to starch. When a diet which was low in starch was given, the child recovered, and he has remained well for the last year.

The criteria given by Andersen for intolerance to starch are: (1) periodic episodes of large, foul stools, (2) a level of amylase in the duodenal juice distinctly below normal, (3) a level of fat in the stools within normal range, (4) excess starch in the stools and (5) a favorable response to a low starch diet. All these criteria are fulfilled in this case except the one concerned with the level of duodenal amylase; this information could not be obtained. The child was intolerant of banana but not of dextrose; this, however, has been true in other types of metabolic diarrhea and cannot be used as a differential factor.

CASE 3.—*Infantile steatorrhea.*

Infantile steatorrhea may be illustrated by the case of A. G., a child who was well until she was 5 months of age, when severe diarrhea consisting of eight to nine stools a day followed a dietary change to unboiled milk. Roentgen examination of the chest showed no abnormality when the child was 9 months of age. The roentgenogram of the gastrointestinal tract was normal. Examination of the stools (by Dr. S. Z. Levine) showed total weight 325 Gm. for three days (very high), water 78.5 per cent (normal) and total fat 39 per cent of the dry weight (high) and indicated that the digestion of starch was good. The patient responded well to the usual high protein diet. After one year a full diet could be given, and the child was completely well at the end of another year under observation.

In the case just described the early age of onset of the diarrhea and the intolerance to fat suggested cystic fibrosis of the pancreas, but the subsequent speedy recovery disproved this diagnosis. The age of onset is lower and the abdominal enlargement and wasting not as severe as in celiac disease. The good digestion of starch and poor tolerance to fat seem to rule out diarrhea due to intolerance to starch. Whether infantile steatorrhea represents an early stage of celiac disease or deserves consideration as a separate entity will require further study.

CASE 4.—*Celiac disease.*

Celiac disease is exemplified by the case of B. C., a child who was well until 11 months of age, at which time large, bulky, foul-smelling, sometimes oily stools were noted. Thereafter no weight was gained for three months and there was gradual enlargement of the abdomen, wasting of the limbs and buttocks and general hypotonicity. Roentgen examination of the small intestine (Dr. William Snow) showed irregularity of the mucosal pattern and clumping of barium in the distended segments. Examination of the stools (Dr. Sobotka, of Mount Sinai Laboratory) showed a total weight of 450 Gm. for three days (very high), water 88.5 per cent (normal under 80 per cent), total fat 45 per cent of the dry weight (normal under 30 per cent), neutral fat 8.5 per cent of the dry weight and fatty acids 36.5 per cent of the dry weight. The analysis indicated that digestion of starch was fair. The fats were evidently well split; the difficulty was in absorption of the split fats, which is typical of celiac disease. Unfortunately, analysis of the duodenal contents, measurement of the serum cholesterol and tests of tolerance to dextrose could not be done. The child did well on a typical high protein diet of protein milk, pot cheese and meat, and later she could tolerate banana. There were two "crises" in which there were sudden watery diarrhea, dehydration and loss of several pounds of weight in a few days. In these episodes the patient responded well to the usual treatment with fluids. The child remained on the high protein diet for approxi-

7. (*a*) Snelling, C. E., and Erb, I. H.: Cystic Fibrosis of the Pancreas, Arch. Dis. Childhood **17**:220 (Dec.) 1942. (*b*) Rauch, S.; Litvak, A. M., and Steiner, M.: Congenital Familial Steatorrhea with Fibromatosis of Pancreas and Bronchiolectasis, J. Pediat. **14**:462 (April) 1939. (*c*) Jeffrey, F. W.: Cystic Fibrosis of the Pancreas, Canad. M. A. J. **45**:224 (Sept.) 1941. (*d*) Harper, M. H.: Congenital Steatorrhea Due to Pancreatic Defect, Arch. Dis. Childhood **13**:45 (March) 1938. (*e*) Daniel, W. A.: Fibrocystic Disease of the Pancreas, Am. J. Dis. Child. **64**:33 (July) 1942. (*f*) Deem, H., and McGeorge, M.: Steatorrhea in Infancy Due to Pancreatic Deficiency, New Zealand M. J. **40**: 155 (June) 1941. (*g*) Wolman, I. J.: Cystic Fibrosis of Pancreas, Am. J. M. Sc. **203**:900 (June) 1942.

mately one year. There has been no relapse during two years in which the patient has been under observation.

CASE 5.—*Allergic celiac disease.*

"Allergic celiac disease" was not mentioned by Andersen,[1] but numerous other workers[8] have reported cases similar to the one which is described in the following paragraphs.

M. S. had been well until he was 3 months of age when he had a slight facial eczema, which responded well to the withdrawal of orange juice and cod liver oil from the diet. At 9 months of age, he had diarrhea with five to six loose stools daily. Roentgen examination of the chest and the gastrointestinal tract showed no abnormality. He did not do well on the usual high protein diet. Examination of stools (by Dr. Sobotka) showed water 72.4 per cent of the total weight (normal), fat 14.7 per cent of the dry weight (normal) and residue of normal digestion of starch. At this time, because of the history of eczema in the patient and of asthma in a collateral branch of the family, cutaneous tests of foods were done. These all gave negative reactions. Thereafter, the patient was put on a diet containing skim milk boiled thirty minutes, without egg, cheese, cream or chocolate. He responded well and has done well in the three years during which he has been under observation since that time.

In this case the normal weight and composition of the stools together with the course of the disease while the patient was on the elimination diet seems to rule out cystic fibrosis, infantile steatorrhea, intolerance to starch and celiac disease. The high percentage of allergic family histories obtainable in cases of all types of metabolic diarrhea adds to the difficulty of diagnosis of this "allergic" diarrhea. This has led many investigators to postulate that the gastrointestinal difficulties originate in an allergic enterocolitis, in which allergic edema of the gastrointestinal mucosa forms a barrier to the absorption of split fats. Since little attention has been paid to the splitting of fats so far in this discussion as compared with the prominence of this feature in other reviews,[9] it may be mentioned that Andersen[1] and others[6] have found the percentages of split fats of little diagnostic significance.

METABOLIC DIARRHEA—THE "CELIAC SYNDROME"

While the literature on the "celiac syndrome" is profuse, only Andersen[1] has attempted classification of the different types correlating clinical characteristics with quantitative chemical examination of the stools. Robbin and Bernhard,[10] in reporting a case of cystic fibrosis of the pancreas, attempted a classification of cases as due to inability to digest starch, fat, protein or substances of more than one of these classes based on the gross character of the stools, but without quantitative analyses. May, McCreary and Blackfan[11] in their valuable study of the effect of the parenteral administration of liver and vitamin B complex in 40 cases of celiac disease, made no attempt to differentiate the various types by adequate analyses of stools. The only change I have made in Andersen's classification is to add the subdivision "allergic celiac" to the variety of metabolic diarrhea. Kunstadter[8a] reported 3 cases in which gastrointestinal allergy produced the celiac type of diarrhea. Cutaneous tests or elimination diets gave positive results; in all 3 cases, although cutaneous tests with milk gave negative results, cow's milk proved the worst offender. Riley[8b] reported celiac symptoms associated with eczema and referred to the syndrome as possibly a metabolic eczema. McKhann, Spector and Meserve[8c] reported 4 cases of celiac syndrome in which the removal from the diet of foods to which the patients gave positive cutaneous reactions produced a cure. Two of the patients showed strongly positive cutaneous reactions to banana, and elimination of banana from the diet was followed by rapid improvement. Unfortunately, these workers too did not do quantitative analyses of stools. As has been mentioned previously, an allergic manifestation seems common in all types of metabolic diarrhea.

Most patients with severe celiac diarrhea, with or without a family history of allergy, do badly on a diet containing whole cow's milk but tolerate boiled skim milk or protein milk. Intolerance to whole cow's milk does not prove the presence of an allergy; it may only indicate inability to digest untreated milk. This reservation is true also for intolerance to other foods as a diagnostic aid.

The importance of routine analysis of stools, not only bacteriologic examination but quantitative chemical analysis for fat and starch, is still too little appreciated. One clinician[12] stressed the point that large fatty stools may occur while a patient is on a fat-free diet and explained this on the ground that the fecal lipids may consist largely of fatty material secreted into

8. (*a*) Kunstadter, R. H.: Gastrointestinal Allergy and the Celiac Syndrome, J. Pediat. **21**:193 (Aug.) 1942. (*b*) Riley, I. D.: Metabolic Eczema in Idiopathic Steatorrhea, Lancet **1**:262 (Feb. 4) 1939. (*c*) McKhann, C. F.; Spector, S., and Meserve, E. R.: Association of Gastrointestinal Allergy with Celiac Syndrome, J. Pediat. **22**:362 (March) 1943.

9. Bodansky, M., and Bodansky, O.: Biochemistry of Disease, New York, The Macmillan Company, 1940, pp. 204-215.

10. Robbin, L., and Bernhard, W. A.: Cystic Fibrosis of the Pancreas, Am. J. Dis. Child. **63**:530 (March) 1942.

11. May, C. D.; McCreary, J. F., and Blackfan, K. P.: Notes Concerning the Cause and Treatment of Celiac Disease, J. Pediat. **21**:289 (Sept.) 1942.

12. Haas, S. V.: Celiac Disease and Its Ultimate Prognosis, J. Pediat. **13**:390 (Sept.) 1938.

the bowels rather than of unabsorbed lipids from food. While this is theoretically true, it obfuscates the entire question. When quantitative studies are made, large decreases in the size of the stool, in the water content and in the percentage of fat are almost always noted when the transition is made from a normal, mixed diet to a diet which is high in protein and low in starch and fat. It was because of this misconception of the importance of the presence of large fatty stools when the diet is free of fat that Haas classified all metabolic diarrhea as celiac disease, and assumed that banana was the cure par excellence. Both Fanconi [4] and Morse [5] had long recognized the different types of the celiac syndrome, those with excessive elimination of fat, those with excessive elimination of starch and those with both. Andersen, by quantitative correlation of the results of examinations of stools, with those of determinations of blood cholesterol, dextrose tolerance tests and determinations of duodenal enzymes, has differentiated the types elaborated. For diagnostic examination the stools of the infant (table) or child are collected for three full days with the patient on a normal mixed diet. Under normal conditions the weight is 40 to 80 Gm. a day, varying with age, the content of water is from 70 to 75 per cent, less than 80 per cent and the content of fat from 10 to 25 per cent of the total; normally there are no free starch granules, although there may be starch in a few vegetable cells. The use of frequent routine analyses of stools in cases of recurrent or chronic diarrhea in infancy and childhood, and the correlation of the results with the clinical picture and with results of determinations of blood cholesterol, tolerance to dextrose and duodenal enzymes when possible, may be confidently expected greatly to increase the knowledge of the numerous types of "metabolic diarrheas." Much light should be thrown on the problems of infant feeding by such numerous, well conducted quantitative studies.

It is my impression that many more cases of metabolic diarrhea are encountered now than in the previous decade. Whether this is due to more adequate recognition or to the present vogue for early institution of solid feedings is difficult to tell. The demonstration that the level of amylase in the duodenal contents is low in infants under 3 months of age suggests that starch should not be added before that age; the demonstration of the occurrence of "allergic celiac" reactions should serve as a note of caution in the routine use of orange juice, cod liver oil and egg yolk, especially raw, at an early age and should perhaps suggest the substitution of the nonallergenic synthetic substances, and the knowledge [13] that administration of the vitamin B complex produces an increase in the duodenal content of lipase may hasten the routine use of this vitamin to prevent development of intolerance to fat. Since most infants with metabolic diarrheas can tolerate fat better than starch, and since they do not usually get enough protein in the solids which are first added to their diets, a slight diminution in the fat of milk, and the addition of more meat and cheese but no cereal seem indicated. If the incidence of metabolic diarrheas in young infants can be decreased by the popularization of high protein, low fat, low starch and high vitamin (especially in A, B complex and D) diets, much good may result.

Stool Analysis, Normal and in Metabolic Diarrheas

	Normal	Cystic Fibrosis of Pancreas	Starch Intolerance	Infantile Steatorrhea	Steatorrhea of Celiac Disease	Allergic Celiac Syndrome
Weight (daily), Gm.	40 to 80	100 to 1,000	100 to 300	100 to 500	100 to 1,000	40 to 80
Water, per cent of total weight	<80	85+	85+	<80	85+	<80
Fat, per cent of dry weight	10 to 25	30 to 80	10 to 25	30 to 50	30 to 50	10 to 25
Starch	Only a few starch grains in vegetable cells	Normal	Free starch grains present	Normal	Normal	Normal

SUMMARY

In an effort to classify recurrent and chronic diarrhea of infancy and childhood on the basis of recent studies the type of metabolic diarrhea known as the "celiac syndrome" has been divided into five subtypes, namely: cystic fibrosis of the pancreas, intolerance to starch, infantile steatorrhea, celiac disease and allergic celiac disease. More frequent chemical analyses of the stools in these cases are advisable. Some changes in our routine feeding of infants would minimize the frequency of these diarrheas. The basis of all infant feeding should be a desire to obviate gastrointestinal complications rather than a desire for "stream-lined infant feeding" in which the avoidance of trouble for the mother is the prime consideration.

1166 Grand Concourse.

13. Piana, G.: Action of Vitamin B_1 on the Pancreatic Enzymatic Activity of Children, abstracted, Am. J. Dis. Child. **59**:1105 (May) 1940.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

THE USE OF "LEITELHO" AS A THERAPEUTIC AND PROPHYLACTIC FOOD IN CHILD HEALTH CENTERS. OSCAR LOBATO, Arch. de pediat. **14**:237 (April) 1942.

The author gives the formula of "Leitelho" and describes the steps in its preparation. This food, which is a mixture of fresh cow's milk, skimmed and acidified, with cream of rice and sugar, is useful and cheap. Lobato reports some cases demonstrating its value.

LOZOYA S., Mexico, Mexico.

SULFONAMIDE THERAPY IN NUTRITIONAL DISTURBANCES. V. ZERBINO, Arch. de pediat. d. Uruguay **13**:597 (Sept.) 1942.

The author has successfully treated the ordinary nutritional disorders accompanied by moderate loss of weight and dehydration but having no toxic manifestations by administration of sulfonamide compounds combined with dietetic management.

All of the patients recovered without exception. In severe dystrophic forms the author has had excellent results from a combination of treatment with sulfonamide compounds with dietetic measures. The mortality in cases of these disorders has been reduced from 40 per cent to 18 per cent. Most of the patients make rapid recovery from the dystrophy, and the use of sulfonamide compounds combined with the dietetic measures seems to increase the rapidity with which they recover.

SCHLUTZ, Chicago.

Vitamins; Avitaminoses

RICKETS REFRACTORY TO VITAMIN D SHOCK THERAPY. JOSÉ MARTINO DE ROCHA, DARCY SOARES and EDMAR BLOIS, J. de pediat. **8**: May-June, 1942.

A baby 14 months old with severe rickets which was refractory to vitamin D shock therapy was observed over a period of one year, with roentgen examinations and laboratory studies. The child died of bronchopneumonia. Single doses of vitamin D, 600,000 international units parenterally and 1,200,000 international units orally, were used with negative results. A total of 10,825,000 international units of vitamin D was used. In cases of this type of rickets the patient should be reexamined every three to four months after treatment, because of the probability of recurrences. Rickets of this refractory type is probably due to associated chronic infections or to diseases of the liver. A comprehensive review of the literature is included.

LOZOYA S., Mexico, Mexico.

Hygiene; Growth and Nutrition; Public Health

REPORT OF A SPEECH SURVEY, HOLYOKE, MASSACHUSETTS. ALICE W. MILLS and HELEN STREIT, J. Speech Disorders **7**:161 (Aug.) 1942.

All of the children in the first three grades were examined by ten examiners, not all of them trained in speech correction. Above the third grade, children were seen who were referred by teachers as being defective in speech. Of 4,685 enrolled in the schools, 10.1 per cent were found to have some defect of speech. While on the average there was a sharp reduction in the total number of defects above the third grade (33 per cent vs. 10.1 per cent), there was a large increase in the number of serious ones in ratio to the total number of defects. A number of other statistical conclusions are of interest. The sex index of speech defects is again confirmed, the greatest variant being in stuttering, in which 5 boys stuttered to 1 female.

PALMER, Wichita, Kan.

BOARDING HOMES. ALVARO BAHIA, Pediat. e puericult. **11**:137 (June) 1942.

The author presents a complete study of the system of caring for orphans and other children who are wards of the state by placing them in private "boarding homes" under governmental contract and supervision. The history of this system and its advantages over other forms of assistance are discussed.

LOZOYA S., Mexico, Mexico.

Prematurity and Congenital Deformities

ARACHNODACTYLY (MARFAN'S SYNDROME). A. A. BARRON, North Carolina M. J. **3**:353 (July) 1942.

Barron reports on a family several members of which had arachnodactyly. The mother and 6 of her children showed the characteristic elongated bony structure. Four of the siblings had ectopia lentis. Of these 4, 1 had a left lateral curvature of the lumbar portion of the spine, while another had had two acute attacks of lymphocytic meningitis and chronic symptoms which seemed to indicate involvement of the central nervous system. There is no proof either that this simultaneous occurrence of meningeal and arachnodactylous symptoms was a coincidence or that the two chronic conditions were linked in close association. The article is illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

Newborn

ASPHYXIA OF THE NEW BORN AND ITS TREATMENT. DELIO AGUILAR GIRALDES, Rev. Soc. pediat. de la Plata **3**:141 (Aug.) 1942.

Of 3,898 infants in the nurseries of the maternity department of the Durand Hospital in Buenos Aires, 80 presented serious disturbances of respiration at birth. The cases were statistically analyzed as to the health of the mother, presentation, length of time in labor, type of labor, sex, size and maturity of the child, nature of the difficulty and treatment. Three types of difficulty were recognized, apnea (13 cases), blue asphyxia (59 cases) and white asphyxia (8 cases). There were 13 fatal cases. Etiologically the cases may be divided into those in which the asphyxia was due to suffocation and those in which it was caused by paralysis. The former group may be subdivided into those in which the cause was a condition of the mother's blood (as infection, anemia, heart disease, uremia) and those in which an interruption of the maternal-fetal circulation (because of difficuty of labor or medication) was responsible. The causes of paralytic asphyxia may be subdivided into external causes (as use of forceps or disproportion of

the pelvis and the fetus) and internal causes (cerebral hemorrhages or malformations). Treatment depends a great deal on a proper evaluation of the cause and type of the asphyxia. The principal features of treatment are (1) relief of obstruction, (2) artificial respiration, (3) administration of gas mixtures, (4) prevention of chilling, (5) and cardiorespiratory stimulation.

HIGGINS, Boston.

Acute Contagious Diseases

THE SMALLPOX EPIDEMIC OF 1797 IN MEXICO. S. F. COOK, Bull. Hist. Med. **7**:937 (Oct.) 1939.

Smallpox was introduced into Mexico by the conquistadors in 1520, and epidemics recurred for about three hundred years, until vaccination was introduced in 1804. After that it never again swept in such devastating epidemics over large parts of the country. Therefore, the last of these prevaccination epidemics, which reached its height in 1797, is particularly interesting.

The author made use of the large amount of documentary information contained in the "Ramo epidemias" of the "Archivo general de la nacion" in Mexico City, which covers the entire official correspondence.

On the basis of this material the author disproves the usually accepted version that the 1797 epidemic can definitely be traced to the importation of smallpox by a ship going from Lima or Callao in Peru to Guatemala and thence to Oaxaca, Mexico. This version was based on a letter from the president of Guatemala to the viceroy Branciforte, dated May 3, 1796. There is no evidence that there was an outbreak of smallpox at Acajutla, the post of arrival, and the disease was present in Oaxaca at that time.

There had been a period of quiescence during the eighties after the extremely devastating epidemic of 1779. By 1790, however, sporadic cases began to appear, which became more frequent in 1793. In the latter year smallpox assumed almost epidemic proportions in Campeche and Tabasco. In 1794 it spread south across the isthmus of Tehuantepec toward Guatemala and crossed to Chiapa, the capital of that Guatemalan province, in October of that year, and then moved farther into Guatemala. The smallpox also spread westward. It is definitely evident from the source material that in 1795 and 1796 there was considerable smallpox in the Chiapas and Tehuantepec region, and "it seems therefore quite reasonable to suppose that the 1797 epidemic, which began in 1796 in Oaxaca, took its origin simply from the pre-existing epidemic in the adjacent provinces of Chiapas and Tabasco" and that the affair of the ship from Lima is of secondary importance, being only an incident having no particular effect on the main events.

Up to 1796 the epidemic followed the trade routes. Originating on the Atlantic coast, it spread over the low pass across the isthmus of Tehuantepec; strict measures prevented it from moving to Mexico City, the other possible route. It did get there, however, after some delay, by way of Oaxaca and Tehuacan. Smallpox broke out simultaneously in July and August 1797 in the cities of Puebla, Orizaba and Mexico. The epidemic spread as far as 200 to 400 kilometers from the Mexico valley, then seemed to grow less in intensity and died out in 1798.

The statistics leave much to be desired. For many areas, especially the wild Indian country, there are no reports at all, and for most smaller towns they are inadequate. They are best for the larger cities, such as Orizaba, Puebla and especially Mexico City, because of the presence of charitable organizations and fairly exact financial accounting; but even for these the figures are far from being exact. After considerable juggling of figures in an effort to overcome the handicap of the many missing data, the author concludes that there was a mortality of about 25 per cent in the province of Oaxaca; using this figure and recognizing "the enormous error involved in such calculations," he estimates that there were 5,000 to 20,000 cases and 1,500 to 5,000 deaths for the same province. In Mexico City the mortality apparently was not much over 10 per cent. The same difficulties are true for the other involved areas. The incidence of the disease was even more difficult to ascertain from the few data extant. However, 20 to 39 per cent of the inhabitants seem to have contracted the disease in some towns, although this epidemic was definitely milder than the previous one, that of 1779. When figures for ages are given, the large proportion of children among those who died of smallpox is evident.

Inoculation had been used little during the 1779 epidemic but was more extensively employed during the epidemic of 1797. "With the unanimous support of the medical profession, a really serious attempt was made to introduce it to all strata of society." The treatment was free to all. At times persuasion bordered on force. In spite of the many disastrous results, inoculation was of definite benefit. With the sparse data available the author tries to show the results. In communities where the mortality from smallpox of persons not given inoculations (naturales) ranged from 8 to 38 per cent, the mortality of those given inoculations (inoculados) ranged from 0 to 11 per cent, the average percentage for seven localities (including Mexico City) being 18.5 and 3.5, respectively, a significant difference "even if we concede considerable error in the data."

The last chapter deals with preventive measures and the difficulties in attempts to carry them out. "For truly it is difficult to imagine a country and a population more ill adapted and more highly refractory to the application of even the rudimentary principles of preventive medicine than 18th century Mexico." It was the duty of any person in an official or semi-official position to report any case to the government, which, directly or indirectly, investigated and ordered such measures as seemed necessary. Only too often the government left the matter in the hands of local authorities, aiding only when requests for help came. The main measures to prevent the spread of the epidemic were quarantine and isolation. Small towns were surrounded and nobody allowed to leave, but at times a town situated in an infected area, but itself free from smallpox, was completely isolated, and nobody was allowed to enter. At times main highways were blocked. All of these measures proved ineffectual, in a large part because of ignorance and actual resistance of the population and in part because of poor cooperation of officials.

Two geographic diagrams and three tables help greatly in the study of this interesting and important article.

ROSENTHAL, St. Paul.

THE ANTIQUITY OF CONGENITAL SYPHILIS. R. C. HOLCOMB, Bull. Hist. Med. **10**:148 (July) 1941.

The author states in a convincing way that the leprosy described by physicians of the Middle Ages is not what is known as leprosy now, but "was syphilis of the center of the face, as now seen to develop in congenital, or, as a late or 'tertiary' symptom of acquired syphilis." The triad of causation of syphilis is unique in being contagious, venereal and congenital. Modern leprosy "has never been proved by any con-

sistently demonstrable means to be infectious, venereal or congenital, or to possess the characteristic visceral lesions seen in syphilis," but the leprosy of the Middle Ages showed the triad of symptoms just mentioned.

Bernard de Gordon's description is typical for that time, and the author presents a translation of the pertinent chapter from the Oxford manuscript of 1348. Bernard explains the hereditary origin of the disease as follows: The embryo contracts it in utero if the father was diseased or if the mother had intercourse with an infected man during the pregnancy; further, the contagion may be acquired through intercourse with a diseased woman, and, in the latent form, a woman who has had intercourse with a diseased man but does not show any symptoms may give the disease to another man.

All these features fit a diagnosis of syphilis. Furthermore, the disease was spread by prostitutes, a fact which again speaks for the diagnosis of syphilis. Several medical authors of the sixteenth century pointed out that "lues venerea" had been described long before their time. As further evidence and absolute proof of his contention, the author brings illustrations of skulls found in the cemetery of an old leprosarium on the Rue de Douai, which are preserved in the Musée Dupuytren in Paris and which have been pronounced "as surely syphilitic as it is possible for skulls to be." (Williams, H. A.: The Origin and Antiquity of Syphilis: Evidence from Diseased Bones, *Arch. Path.* **13**: 779 [May] 1932.)

Vigo's "Surgery" (1514) does not contain the usual chapter on leprosy, a chapter which is usually extensive in any medical book of that time. There is, however, a chapter (the fifth book) on morbus gallicus giving a similar description of the result of venereal infection. The author points out that the epidemics of morbus gallicus mentioned in the late fifteenth and during the sixteenth century did not exist, the reports originating in the confusion of syphilis with many other epidemic diseases; in time "the epidemic Morbus Gallicus became solely a venereal disease under the name lues venerea," and the latter soon split up into gonorrhea and syphilis.

Many sixteenth century physicians touch on such subjects as congenital syphilis and infection of nurses by syphilitic infants, their remarks being similar to those of pre-Columbian authors, though the diseases bear different names.

During the eighteenth century authorities like Jean Astruc and John Hunter disputed the existence of congenital syphilis and considerably retarded its recognition.

"For hardly 150 years has congenital syphilis received the attention . . . it deserved. The greatest progress has been made since the discovery of the Spirochete."

This article, with its clear interpretation of medieval leprosy as syphilis, is most important for the student of the history of congenital syphilis and that of syphilis in general. It destroys what little was left of the theory of the American origin of syphilis.

ROSENTHAL, St. Paul.

"SOMETHING CURIOUS IN THE MEDICAL LINE." REGINALD FITZ, Bull. Hist. Med. **11**:239 (March) 1942.

The author recounts the interesting story of the introduction of vaccination into the United States. Benjamin Waterhouse obtained the first information on this subject when he received a copy of Jenner's *Inquiry* in January 1799, the first copy to be received in America. Coming to the conclusion that vaccination was a most promising procedure, he published a short newsletter in the *Columbian Sentinel* for March 16 of the same year under the title which heads this article. The results were not particularly encouraging. Soon he received Pearson's book of 1798 and presented the matter to the members of the Academy of Arts and Sciences. And when Woodville's "Reports" (1799), backed up by Waterhouse's old and conservative friend Dr. Haygarth of Bath, arrived, he became determined to attempt the experiment.

Vaccine was not obtainable here, and the important question of transmission of the virus from England to America arose. Jenner and his cooperators decided on using threads coated with fresh virus, placed in a tightly closed bottle. This was shipped from Bristol on May 3, 1800, apparently on the Foxwell, which arrived in Boston on July 4. Waterhouse was able to perform the first vaccination four days later on his 5 year old son, Daniel Oliver, which was successful; he was delighted to see the changes of the vaccinia exactly as described by Jenner. Soon he vaccinated more members of his family and household. Not satisfied with this, he repeated Jenner's experiment by having his son Daniel inoculated with matter from a person given inoculation when the disease was in the full-blown stage as well as with a thread coated with matter from a person with ordinary smallpox; moreover, the boy was put to bed with a patient with smallpox. As Daniel remained well, no argument could swerve Waterhouse from his course.

Vaccination spread rapidly, but not everything went smoothly, because of the actions of quacks and other unqualified persons as well as mistaken use of smallpox matter in place of vaccine. This error caused an epidemic at Marblehead and did the cause of vaccination considerable harm. In this predicament Dr. Waterhouse wrote to Jenner by way of his old friend, Dr. Lettsom. Jenner immediately offered advice. There are several letters between Jenner and Waterhouse which are interesting as well as important in the history of the introduction of vaccine to New England. An interesting question raised in one of them was whether cows could be infected with smallpox, prompted by an outbreak of pustular lesions in animals heavily exposed to this disease.

Finally Waterhouse succeeded in producing perfect vaccinations with Jenner's vaccine. The Massachusetts Medical Society, however, did not cooperate. It sent to England for vaccine, but the ensuing vaccinations were failures. The vaccine offered by Waterhouse was not used or acknowledged. "The gentlemen did not choose to be under obligation to me for matter, nor to notice the offer I made them."

In 1802 Waterhouse finished his book on vaccination. The reception in his home state was most discouraging, but England and the South made up for it. From Jenner he received the silver box treasured by the Harvard Medical School Library, truly a present, as Mr. Ring of London expressed it, "from the Jenner of the Old World to the Jenner of the New World."

In 1803 Jenner was made an honorary alumnus of Harvard University with the degree of Doctor of Laws, and Waterhouse sent the diploma to his friend. After this the letters exchanged became progressively fewer and practically came to a standstill during the War of 1812.

The article is illustrated with facsimiles from Jenner's "Inquiry," Waterhouse's broadside on the Kine Pock Institution of Boston, the dedication of Waterhouse's book to Lettsom and Jenner and a photograph of the silver box.

ROSENTHAL, St. Paul.

SURGICAL TREATMENT OF SEVERE ORCHITIS IN MUMPS. CONRAD WESSELHOEFT and SAMUEL N. VOSE, New England J. Med. **227**:277 (Aug. 20) 1942.

Orchitis rarely occurs before the age of puberty, but cases of the condition in prepubescent boys have been recorded. At and above that age, its incidence in mumps is 18 per cent. Collected reports from the literature indicate that under epidemic conditions both testicles are likely to be involved in 1 out of 6 cases.

The rationale of incising the tunica albuginea in severe orchitis is somewhat comparable to that of paracentesis of a bulging, painful drumhead in otitis media. The operation must be done sufficiently early to avoid pressure necrosis in the testicle. An enlarged, hard, tender testicle, with chills and fever, constitutes the indication for surgical intervention. Nitrous oxide and oxygen are the anesthetic of choice. A rise in temperature after operation signifies an invasion of the virus in some other organ.

The end results in 9 cases in which operation was performed in a hospital and in 1 in which the patient was operated on elsewhere are presented. Moderate atrophy took place in the case in which the patient was operated on too late.

GENGENBACH, Denver.

A CASE OF EPIDEMIC CEREBROSPINAL MENINGITIS WITH RECURRENCE. B. ALBAGLI, Arch. de pediat. **14**:425 (Aug.) 1942.

Albagli reports a case of epidemic cerebrospinal meningitis with a recurrence one month after clinical cure. In treating the relapse 1,740 cc. of antimeningococcus serum was used in total, 480 cc. intraspinally and 1,260 cc. intravenously. The patient recovered.

LOZOYA S., Mexico, Mexico.

USE OF DIPHTHERIA ANATOXIN FOR CARRIERS OF VIRULENT STRAINS OF LOEFFLER'S BACILLUS. JOSÉ NOGUEIRA DA GAMA, J. de pediat. **8**:149 (March-April) 1942.

The author reports that after giving injections of diphtheria anatoxin to 13 patients who were carriers of virulent diphtheritic bacilli he obtained negative cultures from 12 of them. The bacilli still present in the one patient gave a negative result when tested for virulence. He suggests the simultaneous use of diphtheritic anatoxin and antitoxin, in any sure case of diphtheria, to prevent the patient from becoming a carrier of virulent bacilli.

LOZOYA S., Mexico, Mexico.

AIRPLANE ALTITUDE FLIGHTS IN WHOOPING COUGH. MILTON CORDOVIL, J. de pediat. **8**:209 (May-June) 1942.

Of 14 patients exposed to high altitude by means of flights by airplane as a treatment for whooping cough, 9 obtained good results, 2 showed improvement and 3 had negative results. The author describes the technic employed and outlines the history of the development of this method of treatment.

LOZOYA S., Mexico, Mexico.

THE TREATMENT OF INFANTILE PARALYSIS DURING THE PERIOD OF RESTORATION AND ORTHOPEDIC PROPHYLAXIS. M. R. MORENO and M. FITTE, Rev. chilena de pediat. **13**:343 (April) 1942.

The authors are convinced of the inefficacy of electrotherapy at any stage in the treatment of infantile paralysis. They report the most favorable experience with restoration of muscular function through disciplined reeducation of affected groups of muscles and their overfunctioning spastic antagonists.

During the early period of the disorder and the period of marked hyperesthesia, hot fomentations are used. Exercises for the reeducation of muscles start immediately after cessation of the febrile period. The gymnastic exercises are carried out while the body is suspended in warm water, which has been properly purified and kept at constant temperature. Restoration can sometimes be accomplished in a relatively short time, and it may take several years to secure satisfactory results.

The authors warn against early orthopedic surgical procedures, such as anastomosis of muscles or transplantation of nerves or tendons. Analysis of muscular function as practiced by North American orthopedic surgeons is the method adopted by their Latin-American colleagues for determining the progress of the treatment.

The authors are of the opinion that surgical procedures should not be undertaken in these cases until at least three years after onset of the disease.

SCHLUTZ, Chicago.

TYPES OF DEFORMITIES FOLLOWING INFANTILE PARALYSIS AS OBSERVED IN THE HOSPITAL ARRIARAN. C. URRUTIA, Rev. chilena de pediat. **13**:371 (April) 1942.

Acute anterior poliomyelitis has so far not occurred in epidemic form in Chile. This disease most commonly attacks children who are near the second year of life. Boys and girls are infected with equal frequency.

The lower extremities are most commonly affected, and of these the right is involved more frequently than the left. About one third of the patients have bilateral involvement.

The author believes that better results are obtained in correction of deformities through operative procedures carried out at the proper time.

Proper provision of such necessary mechanical apparatus as splints for the after-treatment in these cases is a great need in Chile, for which at present there is no adequate provision.

SCHLUTZ, Chicago.

THE TREATMENT OF SCARLET FEVER. FELISA CARBONARI and ELIAS FERRANDO, Rev. Soc. pediat. de La Plata **3**:18 (Jan.-April) 1942.

Four groups of patients with scarlet fever were treated in different ways. To one group scarlet fever immune serum was given; to the second, serum and sulfanilamide; to the third, sulfanilamide, and to the fourth, no medicine. In 14 of 24 patients receiving serum urticaria developed. Renal complications were more common in the patients receiving serum. Suppurative otitis developed in patients in the group receiving no medicine. The initial fever receded soonest in the patients receiving the serum. As the cases were not particularly virulent, deduction as to the best therapy was difficult. Only one of the 79 patients died.

HIGGINS, Boston.

THE TREATMENT OF WHOOPING COUGH. H. E. MERCANTE, Rev. Soc. pediat. de la Plata **3**:173 (Aug.) 1942.

The medications used in the treatment of whooping cough and its complications are discussed. Ten case reports are given. The use of human immune serum seemed to be of value, in the author's experience.

HIGGINS, Boston.

THE COURSE OF MEASLES IN DIABETES MELLITUS OF CHILDHOOD. H. I. BURGOS, Rev. Soc. pediat. de la Plata **3**:196 (Aug.) 1942.

Two children, aged 2¾ and 4⅝ years, with diabetes had measles while under the author's supervision. The course of the measles was no different from that seen in normal children. The children lost between 1 and 2 pounds (0.45 to 0.9 Kg.) in weight; they showed at first an increase in sugar excreted and a mild acidosis and later a tendency to hypoglycemia.

HIGGINS, Boston.

POLYNEURITIS IN A PATIENT WITH WHOOPING COUGH. JULIO C. SANTA MARIA and YEVIL BESEDOVSKY, Rev. Soc. pediat. de Rosario **7**:16 (Jan.-April) 1942.

The authors report a case of polyneuritis due to whooping cough in a child 15 months old; the two lower extremities were affected. Recovery was complete.

LOZOYA S., Mexico, Mexico.

Acute Infectious Diseases

SALMONELLA CERRO, A NEW TYPE OF SALMONELLA. E. HORMAECHE, C. A. PELUFFO and P. L. ALEPPO, Arch. de pediat. d. Uruguay **13**:368 (Aug.) 1942.

The authors describe the characteristics of Salmonella Cerro, a type of Salmonella which was first encountered by them in 1936. It is now established that this form of Salmonella is quite similar to the Salmonella Düsseldorf and Salmonella Arizona described by other authors.

The authors report 13 cases of S. Cerro infection which were observed during an epidemic in the Casa Maternal in 1940. They were able to demonstrate in their studies that this new type of organism is pathogenic for the human species.

SCHLUTZ, Chicago.

PNEUMOCOCCIC SEPTICEMIA ENDING WITH HENOCH'S PURPURA (IDIOPATHIC NONTHROMBOPENIC PURPURA). CESAR PERNETTA and HELIO DE MARTINO, J. de pediat. **8**:223 (May-June) 1942.

A 1 year old baby with pneumococcic septicemia died after an illness of fifty-eight hours. Hemorrhagic spots were present all over the inferior extremities, and the child had a fever, but the platelets and the bleeding and clotting times were normal.

LOZOYA S., Mexico, Mexico.

Chronic Infectious Diseases

INHALATION OF NEBULIZED PROMIN IN EXPERIMENTAL TUBERCULOSIS. ALVAN L. BARACH, NORMAN MOLOMUT and MAX SOROKA, Am. Rev. Tuberc. **46**:268 (Sept.) 1942.

The inhibitory influence of promin (p,p'-diaminodiphenylsulfone-N,N'-didextrose sulfonate) on the development of experimental tuberculosis in guinea pigs has been demonstrated. In this experiment a solution of promin was sprayed in a fine suspension into a closed chamber in which the animal inhaled the nebulized drug for a period of twenty-five minutes. This procedure was repeated daily. As controls, one other group of animals received no medication and to a third group the drug was given by mouth. On comparison with the two control groups it was determined that inhalation of the nebulized spray of promin appeared to have a superior value in that not only was there less tuberculosis in the spray-treated animals but there was less generalized tuberculosis and a far higher survival rate. This in spite of the fact that animals treated by inhalation had a far lower concentration of promin in the blood than the orally fed group. Since it has been shown that nebulized solutions penetrate to the depths of the lungs, it seems possible that a high local concentration of the drug might be obtained in the absence of a high blood level.

EUGENE SMITH, Ogden, Utah.

HISTOPATHOLOGY OF MANTOUX REACTION AND ERYTHEMA NODOSUM. R. VISWANATHAN, Indian J. M. Research **30**:257 (April) 1942.

The author compared the histologic changes of the Mantoux reaction with those of erythema nodosum and found them strikingly similar.

The same cellular reaction, perivascular cuffing and arteriolar and capillary involvement with thrombus formation are seen in both. There is no definite evidence of tuberculoid structure in either. In 2 cases erythema nodosum developed three and five days after Mantoux tests were performed.

LAYMON, Minneapolis. [ARCH. DERMAT. & SYPH.]

THE CLINICAL IMPORTANCE OF SISTO'S SIGN IN THE EARLY DIAGNOSIS OF CONGENITAL SYPHILIS. CELSO DIAS GOMES, Arch. de pediat. **14**:169 (Feb.) 1942.

Sisto's sign (constant crying in a baby that cannot be relieved by all the usual methods and that is provoked or augmented by pressure over the epiphysis) is useful for the early diagnosis of congenital syphilis.

LOZOYA S., Mexico, Mexico.

TUBERCULOSIS INDEX OF CHILDREN IN URUGUAY. PEDRO CANTONNET BLANCH, Arch. de pediat. **14**:495 (Sept.) 1942.

This article presents a study of tuberculosis in the children of the Republic of Uruguay. Special attention is paid to the roentgenographic technic of Manoel de Abreu (Rio de Janeiro, 1936), and a motion is made to call it abreugrafía. The tuberculosis index for children in Uruguay is compared with that in other countries.

LOZOYA S., Mexico, Mexico.

HYPERTROPHIC CERVICAL MENINGITIS OF TUBERCULOUS ORIGIN. R. MATTE, Rev. chilena de pediat. **13**:768 (Aug.) 1942.

The author reports a case of this rare condition in a child aged 7 years. At the time of admission to the hospital the child showed great loss of weight, generalized itching, skin eruption and severe dental caries. The Pirquet reaction was intense. Roentgenographic examination revealed a shadow in the left paratracheal region, due to a moderate glandular enlargement. Six months after admission, a mild attack of measles developed. A week after the disappearance of all symptoms, fever recurred, with severe pain in the superior dorsal region of the spine, at the level of the interscapular space. This was coupled with intense rigidity of the neck. Pressure over dorsal vertebrae from the second to the seventh was painful. There were no indications of meningitis; Kernig's and Brudzinski's signs were negative and there was no headache or vomiting. All lumbar punctures were negative. Roentgenograms showed pronounced enlargement of the left hilar shadow. The sedimentation rate rose from 11 mm. to 35 mm. per hour. These symptoms diminished gradually, but the general condition of the child declined; flaccid paralysis and loss of sensation developed in the right arm; the reflexes of the right leg were exaggerated, and clonus developed, accompanied by a positive Babinski reflex. All symptoms pointed to com-

pression of the medulla at the level of the last cervical vertebra.

Further roentgenographic examination revealed no tumor of the bony structures, and it was concluded that the compressing mass was in the soft parts, probably a tuberculoma or a pachymeningitis tuberculosa localized in the right superior cervical region, compressing the roots of the brachial plexus and, through its effect on the motor area in the medulla, producing the symptoms of a pyramidal disturbance, in the lower extremity. The child finally died of meningeal tuberculosis.

At autopsy a pachymeningitis tuberculosa in the cervical region was found which had caused compression of the medulla at that point. Associated with the condition was extensive left-sided paratracheal tuberculous adenopathy.

SCHLUTZ, Chicago.

Diseases of Blood, Heart and Blood Vessels and Spleen

PERSISTENT COMMON ATRIOVENTRICULAR OSTIUM IN A CHILD WITH MONGOLISM. DAVID W. ROBINSON, Arch. Path. **32**:117 (July) 1941.

Robinson reports the case of a 6 month old white boy, born one month prematurely, who was admitted to a hospital because of fever, cough and diarrhea. His history disclosed "blue spells" at 6 weeks, lack of normal neonatal development and a discharging ear at 3 months. A thoracic roentgenogram at 2 months had disclosed a large heart. When admitted, the child was well developed and nourished but had a mongoloid appearance. He had acute pharyngitis, pulmonary rales, an enlarged heart without murmurs, a cardiac rate of 200, a palpable liver and spleen and a normal hemoglobin content and erythrocyte count. Death occurred during an attack of cyanosis. Autopsy disclosed an opening in the auricular and ventricular septums, common to all four cardiac chambers with two common valves partially closing the lower portion of the ostium, a patent foramen ovale, cardiac hypertrophy and dilatation and evidence of congestion in the viscera. A detailed description of the heart, with two photographs, is given. The extensive bibliography on similar defects emphasizes the common coincidence of congenital heart disease and mongolism; about one half of 39 reported patients in whom interventricular and interauricular defects occurred together were persons with mongolism.

HALLEY, Chicago.

HYPOCHROMIC ANEMIA WITH KOILONYCHIA (SPOON NAILS). B. G. CLARKE, New England J. Med. **227**:338 (Aug. 27) 1942.

A case of idiopathic hypochromic anemia with koilonychia recurring at a seven year interval in a middle-aged man is reported. On each occasion, both the anemia and the spoon nails disappeared completely on treatment with iron.

A survey of the literature reveals that koilonychia is not uncommonly associated with hypochromic anemia of the iron deficiency type and that less pronounced changes in the nails, such as flattening, increased thinness or brittleness and exaggerated longitudinal ridging, are common enough to be of diagnostic help in the disease.

GENGENBACH, Denver.

MODERN CONCEPTS OF THE CLASSIFICATION OF HEMORRHAGIC DIATHESES. MARIO RAVETTA, Arch. de pediat. **14**:245 (April) 1942.

Ravetta reviews the literature on the hemorrhagic diatheses, with special reference to the writings of Spanish authors on hemophilia and thrombopenic purpura (Werlhof's disease). He discusses the experimental evidence as to the action of vitamin C on coagulation time, the disintegration of platelets and capillary resistance, and its therapeutic action in hemorrhagic diathesis. In hemorrhagic diathesis there is no vitamin deficiency in the usual conception but a functional alteration of the metabolism of some of the vitamins (dysvitaminotic theory). This alteration, which can be congenital or acquired, occurs in hemophilia, constitutional purpura and sometimes in scurvy and rickets. In hemorrhagic diathesis there is an alteration of the metabolism of lipids, principally in the adrenals.

LOZOYA S., Mexico, Mexico.

REPORT OF A CASE OF ACUTE CARDIAC INSUFFICIENCY IN AN INFANT. P. DEPETRIS, Arch. de pediat. d. Uruguay **13**:363 (Aug.) 1942.

The author reports a case of acute cardiac insufficiency in a child 2 years of age. It had been well up to the development of this unusual condition. No causative factor could be demonstrated. The child had no renal disease and no acute disorder of the lungs. The disease was apparently not due to a congenital lesion. There had been no previous infection, such as diphtheria, rheumatism, typhoid or scarlet fever.

The blood culture and the Mantoux reaction were negative. There was no parasitic infestation.

The child made a complete recovery.

SCHLUTZ, Chicago.

TOLERANCE TO FREQUENT AND REPEATED BLOOD TRANSFUSIONS IN CHILDREN WITH ANEMIAS. MAMERTO ACUÑA and DARIO V. OROZCO, J. de pediat. **8**:115 (March-April) 1942.

There are real dangers in frequent and repeated use of blood transfusions, but these can be avoided by appropriate prophylactic measures, such as the use of epinephrine hydrochloride (1 per cent), ascorbic acid, sparteine, calcium gluconate and sodium hyposulfite. Headache, fever, vomiting, chills, pruritus, urticaria and shock symptoms are the undesirable reactions observed. It is important to use fresh blood and to be sure that the blood of the donor and that of the receptor are of the same type.

LOZOYA S., Mexico, Mexico.

HYPOCHROMIC ANEMIA IN INFANCY. AFRANIO R. GARCÍA and ARMANDO PENTAGNA, J. de pediat. **8**: 127 (March-April) 1942.

The authors discuss the importance of gastric acidity in the metabolism of iron. They recommend the use of the Katsch-Kalk test to determine gastric acidity and the administration of acid if the result is low.

LOZOYA S., Mexico, Mexico.

CONGENITAL HEMOLYTIC ANEMIA IN A NURSING INFANT. E. G. CASELLI, M. VUCETICH and G. INCHAURREGUI, Rev. Soc. pediat. de la Plata **3**:123 (Aug.) 1942.

A 7½ month old baby had been slightly jaundiced for four months. The liver and spleen were enlarged. The red cell count was 600,000 and the white cell count 20,000; there were 40 per cent reticulocytes and many nucleated red cells. The mother had had biliary colic and jaundice, but there was no other familial disease. Splenectomy was being considered.

HIGGINS, Boston.

Diseases of Nose, Throat and Ear

EFFECT OF TONSILLECTOMY ON RESPIRATORY INFECTIONS IN CHILDREN. ALBERT D. KAISER, Bull. New York Acad. Med. **18**:338 (May) 1942.

In this paper the term "respiratory infection" includes all of the symptoms primarily and secondarily referable to the upper respiratory tract. Though children of all ages may contract any of the infections of the respiratory tract, all of these infections are most prevalent among 3 to 7 year old children. In evaluating the effects of tonsillectomy, the author has taken into consideration all the factors which influence the development of infections of the respiratory tract.

The author stresses the fact that no scientific evidence is as yet available which explains the part that the tonsillar tissue plays in the economy of the child. Four thousand, four hundred children were followed for ten years. One-half this number had their tonsils and adenoids removed; the other half did not. The initial observation of these children began when they were between the ages of 4 and 7 years and continued into their high school period. At the time of their initial examination indications for tonsillectomy were numerous but in general the same for the entire group. For various reasons, one-half the total group submitted to the operation, so that the children who were not operated on served as controls.

Tonsillitis was a common complaint among the young children. Approximately 38 per cent of the entire group were subject to repeated attacks of tonsillitis during the first seven years of life. The incidence of sore throat was lessened during the ten year period, and among children receiving surgical treatment attacks of tonsillitis occurred with only a slight decrease in frequency during the same years. The author concludes that the common ailment named tonsillitis or sore throat occurred less frequently among the patients whose tonsils had been removed.

Common Cold.—Four colds or more a year per child occurred with about equal frequency in both groups. Forty-two per cent of the children were subject to this repeated infection up to the age of 7 years. Over the ten year period the children who had been operated on showed only a slight diminution in comparison with the children who had not had surgical treatment. But it is likely, the author states, that the removal of the adenoids benefited the younger children. As the children advanced in age the adenoid tissue retrograded, so that those who had not been operated on were likewise benefited. The trend, as far as frequent colds were concerned, was downward as the child progressed in age. There is insufficient evidence to show that the role of the tonsils is a significant one either in predisposing to the common cold or in preventing it.

Otitis Media.—Only purulent otitis media was considered in this study. Fifteen per cent of the children who were subsequently operated on had suffered from this disease before they were 5 to 7 years of age. In the control group 12 per cent were thus affected. During the three year period after removal of tonsils and adenoids the incidence of otitis media was considerably lower in the group that had received surgical treatment.

Cervical Adenitis.—Cervical adenitis is usually secondary to nasopharyngeal infection. In each group 15 per cent of the children had enlargement of the cervical glands before they were 5 to 7 years of age. During the three year period after tonsillectomy, the incidence of cervical adenitis among children who were operated on was 5 per cent; among those not operated on the incidence was 14 per cent.

Sinusitis and Nasal Allergy.—Children with acute sinusitis and nasal allergy were, from this study, not favorably influenced by tonsillectomy.

Laryngitis.—Recurrent laryngitis was observed in 3 per cent of the children after the operation and in 5 per cent before the tonsillectomy.

Bronchitis and Bronchopneumonia.—Generally, tonsillectomy reduces the incidence of infections of the upper respiratory tract, but it does not tend to lower the number of infections of the lower respiratory tract.

JAHR, Omaha.

FUNCTIONAL SPEECH AND VOICE DISORDERS. JAMES S. GREENE, J. Nerv. & Ment. Dis. **95**:299 (March) 1942.

Stuttering is a symptom the genesis of which is in the emotional stream rather than in the vocal structures, and treatment, to be successful, must be directed toward the whole personality pattern. Reeducation of muscles of speech, however, is at times an important phase of therapy. The whole problem of stuttering is comprehensively discussed. The author bases his ideas and conclusions on personal experiences in over 20,000 cases.

JAHR, Omaha.

THE ETIOLOGY OF STAMMERING. ELMER L. KENYON, J. Speech Disorders **7**:97 (Aug.) 1942.

Vocal cord adduction is a life-saving function. Voice production is a modification of adduction. In developing mental imagery for control of the vocal cords, a child may, under stress of confusion, mental excitement or emotional strain, develop an imagery of complete cord adduction as being the way to produce voice. Thus a complete but transient block develops on phonation, which is the fundamental symptom of "stammering." Other symptoms are caused by social pressures of ridicule and embarrassment on the child. The author considers his theory proved by the pragmatic test of no failures under a treatment designed to draw the child's attention to proper vocal production. For more than seven years of work, he had no failures with children between the ages of 8 and 12 years. The author states that these are the most favorable ages for the program of treatment that he designed. Manner of treatment, number of cases and methods of control are not discussed by the author in this article.

PALMER, Wichita, Kan.

Diseases of Lungs, Pleura and Mediastinum

VIRUS PNEUMONIAS: I. PNEUMONIAS ASSOCIATED WITH KNOWN NONBACTERIAL AGENTS: INFLUENZA, PSITTACOSIS AND Q FEVER. MAXWELL FINLAND and JOHN H. DINGLE, New England J. Med. **227**: 342 (Aug. 27) 1942.

This report deals with the various pneumonias considered to be of nonbacterial origin and is divided into two parts. In the first, the authors present a review of the recent studies dealing with nonbacterial pneumonias associated with known virus or rickettsial agents; these include, chiefly, influenza, psittacosis and Q fever. The second part will contain a description of atypical pneumonias of unknown origin and a review of the attempts to identify a causative agent in such conditions.

In the influenza epidemics of 1890 and 1918, the influenzal bacillus of Pfeiffer was thought to be the causative factor, with the streptococcus and the staphylococcus acting as complicating factors.

It is now generally accepted that some filtrable virus was probably the causative agent in most of the widespread epidemics of typical influenza that have occurred in the last few years. This virus has been labeled "influenza A virus." In smaller and more localized outbreaks, another virus, now called "influenza B virus," was found to be the cause, and there is indirect evidence that possibly a third one and perhaps still others give rise to the characteristic clinical picture in some limited outbreaks.

Pneumonia may appear in patients with influenza during the height of the original attack, or it may have its onset after a varying interval, following apparent recovery from the influenza. A human disease, resembling influenza on the one hand and typhoid on the other and associated primarily with atypical pulmonary lesions and acquired from sick parrots, has been known since 1880.

The virus of psittacosis and the related viruses are rather large and pass only the coarser bacterial filters. They have many morphologic and other characteristics of rickettsias, but no arthropod vectors have been established. Rashes do not occur regularly in psittacosis.

Pulmonary lesions, however, have been recognized as part of the clinical and pathologic picture of severe rickettsial diseases, notably in typhus and in Rocky Mountain spotted fever. Pulmonary complications have recently been reported in cases of South African tick bite fever, another of the known rickettsial diseases.

In 1937, Derrick described a new pathologic entity occurring in the state of Queensland, Australia, and gave it the name of "Q fever." Derrick named the causative factor Rickettsia burneti. In the spring of 1935, Davis and Cox, working in the laboratory of the United States Public Health Service at Hamilton, Mont., described a filter-passing agent obtained from a group of ticks of the species Dermacentor andersoni. Cox suggested the name Rickettsia diaporica to emphasize its filtrability. No pulmonary signs or symptoms were mentioned.

An outbreak of so-called "pneumonitis" ascribed to the agent of Q fever occurred among employees of the National Institute of Health, in Washington, D. C. The clinical features and the conditions observed on physical and roentgen examinations in these cases were similar to those of the various atypical pneumonias currently reported from various parts of the United States.

GENGENBACH, Denver.

CONTRIBUTION TO THE STUDY OF THE ETIOLOGY OF BRONCHOPNEUMONIA IN INFANTS. ARGEO POUCHÉ, Arch. de pediat. **14**:391 (July) 1942.

Sixty cases of bronchopneumonia (primary) were studied, and practically all of them were found to be monomicrobic; pneumococci (particularly type IV) and hemolytic streptococci were the organisms most commonly found. Cultures were made with blood and with material from the pharynx, lung and pleura, but the most reliable results were those of material obtained by puncture of the lung. The difference in results reported from studies of the causation of primary bronchopneumonia are due to the different technics employed in the collection of samples; this can be proved by using the three different technics mentioned.

LOZOYA S., Mexico, Mexico.

TRANSITORY FLEETING PULMONARY SHADOWS. R. MATTE and O. CORREA, Rev. chilena de pediat. **13**: 415 (May) 1942.

The mechanism of the development of these shadows is due to a combination of inflammatory pulmonary processes. There may be alveolitis, bronchial obstruction, atelectasis and areas of pulmonary edema, possibly of allergic origin. Characteristic roentgenologic and clinical symptoms ensue from such developments.

These shadows generally disappear within a period of two months. They must be differentiated from shadows due to tuberculous pulmonary involvement. The tuberculin test, determination of the sedimentation rate of the erythrocytes and rigorous bacteriologic examination of sputum and stomach washings are the chief aids in establishing this differentiation. Other aids are a minute check of the antecedents and the history of the beginning of the process and its subsequent development. The authors point out that tuberculous shadows can at times be ephemeral and that a tuberculous process may undergo complete absorption and apparently disappear within two or three months.

A tuberculous infection, dormant or acutely active, may cause sensitization of adjacent tissues which may make these areas susceptible to other forms of inflammation, nonspecific and nontuberculous. The fleeting shadows may be the result of such inflammations.

SCHLUTZ, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE EFFECT OF CARMINATIVES ON THE EMPTYING TIME OF THE NORMAL HUMAN STOMACH. EDWARD J. VAN LIERE and DAVID W. NORTHUP, J. Pharmacol. & Exper. Therap. **76**:39 (Sept.) 1942.

The discordant results, experimental and clinical, from the use of carminatives are well known. Fluidextract of ginger, tincture of capsicum and oil of peppermint were tested on the gastric emptying time of cereal mixed with barium sulfate given to 20 normal young men. In one of six trials with ginger and one of nine with capsicum there was a significant decrease in gastric emptying time, but peppermint had no effect. The results indicate that so far as gastric emptying time is concerned these carminatives have value in exceptional cases only.

PILCHER, Cleveland.

EPIDEMIOLOGY OF DIARRHEA IN NEW YORK CITY. SAMUEL FRANT, New York State J. Med. **42**:1911 (Oct. 15) 1942.

This paper is one of four in a symposium on diarrhea.

In 1941 there were 341 confirmed cases of bacillary dysentery in New York city. Outbreaks in institutions were especially frequent, as they had been also in previous years. Amebic dysentery is not necessarily a tropical disease, as in 5 out of 45 cases reported the persons had never been out of the city. Some thousand cases of food poisoning occur each year. Smoked fish, custard-filled pastries and improperly refrigerated meats and salads have frequently caused infection.

Since 1934 epidemic diarrhea of the newborn has appeared in and around New York city. In the past eight years, 75 outbreaks have occurred in 40 maternity institutions. This form of diarrhea is a distinct clinical entity, occurring in newborn infants, characterized by severe diarrhea, dehydration and toxicosis. The cause is still unknown. During the seven years preceding 1941, the mortality had been nearly 50 per cent, but in that year the fatality rate dropped to 18 per hundred.

All cases of infectious diarrhea should be carefully investigated by health departments and laboratories.

AIKMAN, Rochester, N. Y.

A Case of Exomphalos Successfully Treated by Operation. Leonard Ley, Brit. J. Surg. **30**:168 (Oct.) 1942.

Ley reports a successful operation on a 10 hour old infant with a large hernia into the umbilical cord. The sac contained the whole liver and a large proportion of the abdominal contents.

Brick, Toronto, Canada.

Achalasia of Childhood. C. H. Wesley, M. J. Australia **2**:477 (Nov. 28) 1942.

The author presents a short discussion of cardiospasm, pyloric stenosis, duodenal ileus and megacolon.

Gonce Jr., Madison, Wis.

Treatment of Stomatitis Aphthosa with Nicotinic Acid: Three Cases. E. Corrêa de Azevedo and Humberto Baía, Arch. de pediat. **14**:127 (Jan.) 1942.

Three patients with stomatitis aphthosa were successfully treated with 200 mg. of nicotinic acid given orally on each of two days, after failure of treatment with ascorbic acid and sulfanilamide. The authors believe that the infection appears in subclinical cases of vitamin deficiency and that nicotinic acid hinders the growth of the bacillus in the mucosa.

Lozoya S., Mexico, Mexico.

Acute Intestinal Infection with No Specific Lesions of the Intestine. Eugenio Cienfuegos, Arch. de pediat. **14**:139 (Jan.) 1942.

The author calls attention to the fact that there are clinical entities resembling intoxication which are not cured by the usual treatment and are not evidenced by any specific lesions of the intestine. These syndromes are infectious gastroenteritis, catarrhal bronchoenteritis and pseudotyphoid enteritis.

Lozoya S., Mexico, Mexico.

Infectious Diseases with Specific Lesions of the Intestinal Tract. Eugenio Cienfuegos, Arch. de pediat. **14**:173 (Feb.) 1942.

The author describes follicular enterocolitis (known in some other countries as acute mucohemorrhagic colitis), rectosigmoiditis and typhoid in babies, with its peculiar symptoms and its treatment.

Lozoya S., Mexico, Mexico.

Infection and Sulfonamide Therapy in Digestive Disturbances and Enteritis of Infancy. V. Zerbino, Arch. de pediat. d. Uruguay **13**:517 (Sept.) 1942.

The authors, on the basis of considerable clinical experience, believe that the dysenteric enteritis caused by the organisms of Shiga, Flexner, Sonne and Hiss, which today are such a serious problem in subtropical zones and are the causative agents in probably 40 per cent of the cases of infantile diarrhea, can be entirely cured through treatment with sulfathiazole, sulfaguanidine or sulfadiazine. The Salmonella forms of enteritis do not respond quite as well to these drugs, but in the treatment of such infections sulfapyridine, sulfathiazole and sulfadiazine may all be successful.

Sulfanilamide is efficacious for the streptococcic forms of enteritis. In the staphylococcic form, sulfathiazole is effective as well as in enterococcic enteritis or that due to Bacillus proteus.

The authors found that the daily dose of sulfathiazole of 15 Gm. per kilogram body weight does not assure effective concentration of the free drug in the blood of the child with diarrhea. Higher dosage must be given, up to 30 or 40 Gm. per kilogram of body weight and sometimes even higher, during the first day of the treatment of the severe diarrheal condition or a colic form of enteritis. The dosage can be reduced about the third day after the diarrhea has improved. The concentration of the drug in the blood must be determined on the second or third day of the treatment, because at that time the concentration will be stabilized.

Schlutz, Chicago.

A Case of Riga-Fede Disease. Oscar Texeira da Matta and Ernani Mercadante, J. de pediat. 8: 139 (March-April) 1942.

This is a report of a case of Riga-Fede disease (sublingual, ulcerated fibroma, granuloma or papilloma) treated with different antiseptics and finally by surgical excision. The patient recovered. A comprehensive review of the literature on the subject is included.

Lozoya S., Mexico, Mexico.

Sulfathiazole in Treatment of Dysenteriform Enterocolitis in Infants. Olavo Lustosa, J. de pediat. **8**:157 (March-April) 1942.

In Juiz de Fóra, Brazil, dysenteriform enterocolitis is principally causd by Bacillus coli, according to stool cultures. The author suggests the use of sulfathiazole in all cases of dysenteriform enterocolitis, and even in cases of dyspepsia and toxicosis, because these would always be followed by infections.

Lozoya S., Mexico, Mexico.

Intussusception. Alipio Pernet, Pediat. e puericult. **11**:32 (Sept.-Dec.) 1941.

Pernet discusses intussusception with special reference to that due to the presence of Ascaris lumbricoides.

Lozoya S., Mexico, Mexico.

Von Gierke's Disease [Glycogenosis]: Report of a Case. H. Henriquez G., Rev. chilena de pediat. **13**:646 (July) 1942.

The author reports a case of glycogenosis occurring in an infant 1 year and 7 months old.

Enlargement of the abdomen had been noticed by the mother since the infant was 9 months old, and a globular form of the abdomen had existed since birth. There was prolonged persistence of high values for blood sugar after the ingestion of carbohydrate, and the blood sugar curve was not altered by injection of epinephrine hydrochloride. There were no symptoms of circulatory or biliary obstruction. A pronounced increase in lipemia was noted.

There is no treatment for the condition, and all cases so far reported have terminated fatally.

Schlutz, Chicago.

The Infectious Factor in Infantile Cholera: Its Treatment by Sulfapyridine. Jorge Munos Turnbull, Rev. mex. de pediat. **12**:201 (June) 1942.

The essential factors in infantile cholera are three: (1) malnutrition, (2) dehydration and (3) infection.

Supplying of liquids is essential, as well as combating other infections and the symptoms which make up the syndrome of cholera in infants.

Before using sulfapyridine, the author feared that it might cause toxicity, but he used small doses with good results.

Six cases are reported.

Giffen, Toledo, Ohio.

Nervous Diseases

CONGENITAL ANOMALY OF THE CEREBELLAR VERMIS. A. L. SAHS, Arch. Path. **32**:52 (July) 1941.

The case of a 16 year old boy with a cerebellar anomaly is reported because of the rarity of the lesion and because of the clinical simulation of a tumor in the posterior fossa. The patient suffered from epileptic seizures and from dizziness after exertion and changes in position; he was admitted to a hospital because of acute symptoms developing after a neck-strengthening contest. At operation he was observed to have an apparent defect of the vermis with a greatly enlarged fourth ventricle full of cerebrospinal fluid; preoperative spinal tap had revealed no increase in pressure. Autopsy disclosed a moderate internal hydrocephalus, generalized flattening of the gyri and narrowing of the sulci and displacement and compression of the occipital lobes, the splenium of the corpus callosum and the vermis of the cerebellum. The vermis was present in rudimentary form with all of its major divisions. Failure of the vermis to close the fourth ventricle completely and accumulation of cerebrospinal fluid in the fourth ventricle and over the cerebellar hemispheres undoubtedly were responsible for the symptoms preceding death. A possible embryologic explanation is given for the malformation. A review of the literature and six photographs are included.

HALLEY, Chicago.

MEBARAL IN THE TREATMENT OF EPILEPSY. BENJAMIN COHEN and ABRAHAM MYERSON, New England J. Med. **227**:336 (Aug. 27) 1942.

After discussing previous reports on the use of mebaral (methylethylphenobarbital) Cohen and Myerson report the results of its use on a group of controlled patients with epilepsy at the Grafton State Hospital, Massachusetts. This group had been under other forms of treatment for from six months to three years.

The authors found that the drug is particularly useful for treatment of epileptic children, who prefer tasteless medication, of psychotic epileptics who must be treated by medication concealed in their food, and of patients who cannot be given adequate phenobarbital because of toxic drowsiness and, finally, for trial with patients who do not show satisfactory response after trials of phenobarbital, diphenylhydantoin sodium and bromides, separately or in combination.

Mebaral was found to be less productive of toxic symptoms than phenobarbital or diphenylhydantoin sodium, and proportionately higher dosage was continued with safety and with as great or greater clinical effectiveness.

GENGENBACH, Denver.

EXTRADURAL HEMORRHAGE. FRANCES C. ANSANELLI and JACOB MESHKEN, M. Rec. **155**:403 (Aug.) 1942.

Extradural hemorrhage, that between the inner table of the skull and the external layer of the dura, is known also as epidural, supradural and middle meningeal hemorrhage. The usual cause is trauma, and the vessel most commonly involved is the middle meningeal artery or vein.

Clinically the symptoms fall into one of the following three groups, though many cases are not typical:

1. A head injury followed by sudden unconsciousness, a lucid interval of from hours to a few days and then a relapse into unconsciousness. This is the classic picture.

2. A head injury followed by no unconsciousness and then, in a short period, stupor or dizziness which gradually proceeds into unconsciousness.

3. A head injury followed by sudden onset of semiconsciousness or unconsciousness which persists and progresses, with or without additional focal signs.

A history of one of these groups of symptoms, with the development of focal signs, establishes the diagnosis. As a rule, the history and physical observations, rather than a roentgen examination, are the most important diagnostic factors, however, roentgenograms are valuable when a fracture can be demonstrated in a patient who becomes suddenly unconscious after a head injury, with no focal signs. Examination of the spinal fluid is of least importance.

Surgical treatment is indicated the moment the diagnosis is made, so that the clot may be removed and the bleeding point controlled.

Three cases which do not follow the classic course are reviewed.

FERDINAND, Peoria, Ill.

FATAL INTRACRANIAL VENOUS HAEMATOMA FOLLOWING VENTRICULAR DRAINAGE. J. SCHORSTEIN, J. Neurol. & Psychiat. **5**:142 (July-Oct.) 1942.

Schorstein reports 3 cases in which death resulted from intracranial hemorrhage after ventricular drainage. In all 3 cases chronic internal hydrocephalus with increased intracranial pressure was present, caused in 2 instances by obstruction of the aqueduct near its commencement and in the third case by adhesive arachnoiditis blocking the foramen of Magendie. In the first 2 instances the hemorrhage was extradural, while in the third it was subdural and intracerebral. The bleeding was probably of venous origin, derived from the rupture of dural veins. In all 3 cases the extracerebral clots overlay the frontal lobes. The author attributes the hemorrhages to the reduction of intracranial pressure by the ventricular drainage. This decreased pressure causes the dura to become detached from the bone and, aided by traction on the dura by way of the venous anchorage of the brain, results in rupture of veins passing between the dura and the skull. The venous pressure, which exceeds the cerebrospinal fluid pressure when drainage is instituted, aids still further the expansion of the clot from the ruptured veins. Young persons with chronic hydrocephalus are the ones most likely to have a complication.

MALAMUD, Ann Arbor, Mich.
[ARCH. NEUROL. & PSYCHIAT.]

A CASE OF PNEUMOCOCCIC MENINGITIS TREATED WITH SULFATHIAZOLE. LAGES NETTO, J. de pediat. **8**:67 (Jan.-Feb.) 1942.

An 18 month old baby with pneumococcic meningitis (positive spinal fluid culture) was treated with a total of 28 Gm. of sulfathiazole, by mouth. The fever abated after seven days of treatment, and negative cultures were obtained on the eighth day. The child recovered.

LOZOYA S., Mexico, Mexico.

CONVULSIONS IN INFANTS. MARTAGÃO RAYMUNDO CESTEIRA, J. de pediat. **8**:235 (May-June) 1942.

In studying convulsions in infants it is very important to know the familial and individual histories and to note the types of convulsions, the associated symptoms, the sequelae and the results of various treatments. Convulsions in infants are nothing more than a symptom, and so classification of them as disease entities has no real basis.

LOZOYA S., Mexico, Mexico.

TREATMENT OF SPASTIC DIPLEGIA OR LITTLE'S DISEASE. A. JOHOW, Rev. chilena de pediat. **13**:337 (April) 1942.

Today the most important part of the treatment of these spastic diseases consists in gymnastics and massage. All brusque therapy or procedure produces immediate reflex action in patients with these disorders, which results in aggravated contraction of all the musculature and hinders every effort at passive exercise.

Only with great patience and a reeducation of muscles extending over a period of years can these patients be helped, although in most cases they are never completely cured. The facilities of the average hospital are usually not adequate in the treatment of these diseases. Special institutions with special equipment are desirable. Unfortunately, such institutions do not exist at the moment in Chile.

SCHLUTZ, Chicago.

A REPORT OF SIX CASES OF TUMORS OF THE SPINAL CORD OCCURRING IN CHILDHOOD. R. OLEA G., Rev. chilena de pediat. **13**:629 (July) 1942.

The author reports 6 cases of a condition which is comparatively rare in children. The ages of the patients ranged from a few months to 10 years.

A history of a rapidly growing mass, with the development of flaccid palsies, generally indicates the presence of a malignant tumor. Important factors in the physical diagnosis are the demonstration of focal lesions in the spinal medulla by motor and sensory tests, the demonstration of obstruction of the vertebral canal by Queckenstedt's test, the presence of malignant tumors in other parts of the body and the evidence from roentgenography with iodized poppyseed oil. Syphilis, tuberculosis of the vertebrae, other infections and trauma must be excluded.

The treatment is surgical intervention, generally combined with high voltage roentgen therapy. The results are often brilliant, especially in cases of benign tumors.

SCHLUTZ, Chicago.

A CASE OF STREPTOCOCCUS MENINGITIS IN A NURSING BABY, WITH RECOVERY. E. G. CASELLI, Rev. Soc. pediat. de la Plata **3**:81 (Jan.-April) 1942.

A nonhemolytic streptococcus meningitis developed in a 7 month old boy after a slight nasal cold; after eleven days of treatment with sulfanilamide, the spinal fluid became normal and the child seemed well again. Eleven days later the child had a relapse, and only after five and a half weeks was the spinal fluid again normal. The dose of sulfanilamide given in the first attack was 25 cg. per kilogram of body weight, and in the relapse 40 cg.; during the relapse an intraspinal injection of sulfanilamide was given also.

HIGGINS, Boston.

Psychology and Psychiatry

EPITOME OF AGNOSIA, APRAXIA, AND APHASIA WITH PROPOSED PHYSIOLOGIC-ANATOMIC NOMENCLATURE. J. M. NIELSEN, J. Speech Disorders **7**:105 (Aug.) 1942.

The author presents a review of present theory concerning the aphasias and a comprehensive outline of a proposed new terminology on a more exact and usable anatomic-physiologic basis.

PALMER, Wichita, Kan.

IMPORTANCE OF SENSORY TRAINING IN SPEECH THERAPY. SAMUEL D. ROBBINS, J. Speech Disorders **7**:183 (Aug.) 1942.

The author reviews the brief literature on auditory memory span and presents the results of a study of digit auditory memory span, phonemic auditory memory span and syllabic auditory memory span on children with defective speech—sound substitutions (81 subjects), elisions (76 subjects) and delayed speech (33 subjects). The results are reported for age groups of 4 to 6 years, 7 to 9 years and 10 to 13 years. In all three types of defects the results approach the normal results of digit auditory memory span. However, 13 per cent of children with sound substitutions, 33 per cent of those with elisions and 45 per cent of those with delayed speech had definitely short auditory spans. The author emphasizes the importance of attempting to lengthen the auditory memory span in children with these defects and suggests methods of teaching speech to those whose spans do not seem to lengthen.

PALMER, Wichita, Kan.

THE EFFECT OF DRUGS ON BEHAVIOR AND THE ELECTROENCEPHALOGRAMS OF CHILDREN WITH BEHAVIOR DISORDERS. D. B. LINDSLEY and C. E. HENRY, Psychosom. Med. **4**:140 (April) 1942.

Lindsley and Henry report on the electroencephalograms and behavior ratings of 13 children with behavior disorders who were studied over a period of six weeks. Amphetamine, phenobarbital and diphenylhydantoin sodium were used, and the results show that the behavior improved notably with amphetamine medication. Decided improvement of behavior also occurred with diphenylhydantoin, but this drug was less effective than amphetamine. Phenobarbital when given after a period of amphetamine medication caused exacerbation of symptoms, but when given after an initial control period it produced insignificant changes in behavior.

The electroencephalograms showed a number of statistically significant changes, but these were not pronounced and were not proportionate to the changes in behavior produced by the various drugs. The electroencephalographic changes were not always consistent for any one subject, for any one area of the head or for any one drug, when similar changes in behavior were noted. Therefore, the authors conclude that behavior disorders in children presumably have some relation to the abnormalities observed in the electroencephalograms, but that improvement in behavior may occur without any essential modification in the abnormal electrical activity of the cortex.

SCHLEZINGER, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

STUDY OF EMOTIONS AND MENTAL STATES IN INFANTS. JOSÉ FLORES MUÑOZ, Arch. de pediat. **14**:433 (Aug.) 1942.

The author insists on the importance of this study in pediatric practice in order to have children who are healthy both physically and mentally. It is necessary to consider the emotions and mental states in treating children with physical defects, speech defects, mental retardation, hyperemotivity, jealousy and maladjustment to family relationships.

LOZOYA S., Mexico, Mexico.

Diseases of the Genitourinary Tract

THE SECRETION OF URINE BY DEHYDRATED AND NORMAL INFANTS. W. F. YOUNG and R. A. MCCANCE, Arch. Dis. Childhood **17**:65 (June) 1942.

Infants aged 1 to 8 months have kidneys which are intermediate in functional capacity between those of adults and those of newborn children. They have lower rates of glomerular filtration and lower clearances of urea than adults, expressed on the basis of surface area, and both of these measurements vary with the volume

per minute at normal rates of urinary flow. The clearances of minerals also tend to be lower than in later life. The amount of solids in the urine does not rise, as in adults, when the volume per minute falls. No evidence has been obtained that children who have been dehydrated by diarrhea or vomiting have a specific renal lesion. Their kidneys are functioning in the normal infantile manner, and the chemical abnormalities in their serum are due to the small amount of water available for excretion. KELLY, Milwaukee.

MENARCHE IN RELATION TO CLIMATE. B. ALBAGLI, Arch. de pediat. **14**:207 (March) 1942.

The author reviews the literature on the subject and reports on a study of menarche in 1,000 women. The menstrual function develops early in the tropics. This precocity is not related to constitutional type. Menarche occurs earlier in Negro women than in white women.

LOZOYA S., Mexico, Mexico.

GLOMERULONEPHRITIS: SOME CASES TREATED WITH SULFANILAMIDE. ELYSIO ATHAYDE, Pediat. e puericult. **11**:165 (June) 1942.

The author reports his results in treating about 20 patients with glomerulonephritis with sulfanilamide, including detailed histories of 5 cases. Tolerance to the drug was good, and treatment with it induced rapid regression of the edema and fever. The urine was normal within a few days.

LOZOYA S., Mexico, Mexico.

OMBREDANNE'S SYNDROME (POSTOPERATIVE SHOCK) IN AN INFANT AFTER AN OPERATION FOR TORSION OF THE CORD. E. C. ERZI, Rev. Soc. pediat. de la Plata **3**:103 (Aug.) 1942.

Ombredanne described in 1922 a type of surgical shock usually occurring six to twenty-four hours postoperatively and characterized by hyperthermia (39 to 41 C.; 102 to 106 F.) and pallor.

Erzi reports a case in a 6 month old boy who was operated on for torsion of the spermatic cord with gangrene of the testicle. The operation was performed with the patient under ether anesthesia four days after the torsion was manifest; twenty-six hours later the child had a temperature of 40.2 C. (104.4 F.), extreme pallor, blue circles under the eyes, uncountable pulse, hypotension and rapid respiration. Treatment was symptomatic and consisted of hydration with salt and sugar solutions, sublingual administration of epinephrine, enteroclysis with a sodium bicarbonate solution, cold packs and enemas. The temperature and circulation were normal twenty-four hours later. Prophylaxis before and during operation is even more important than treatment after the syndrome appears.

HIGGINS, Boston.

Diseases of the Ductless Glands; Endocrinology

EXOPHTHALMIC GOITER OF THE JUVENILE TYPE. RALPH R. MOOLTEN and MAURICE BRUGER, Arch. Surg. **45**:622 (Oct.) 1942.

The extensive literature on juvenile exophthalmic goiter is reviewed. The condition occurs infrequently in children. Clinically, the juvenile resembles the adult type, and in the early stages either type is frequently overlooked, especially when exophthalmos is not well developed. The immediate effects of subtotal thyroidectomy are as beneficial in juvenile exophthalmic goiter as in the adult type; it is the ultimate result that is often in doubt. The operative handling of juvenile patients presents a controversial problem. The authors' practice is to leave little gland, using the same technic as is used for adult patients.

KAISER, Rochester, N. Y.

RELATION OF THYROID TO MAMMARY GLAND STRUCTURE IN THE RAT WITH SPECIAL REFERENCE TO THE MALE. J. FREDERICK SMITHCORS and SAMUEL L. LEONARD, Endocrinology **31**:454 (Oct.) 1942.

The general effects of thyroidectomy on mammary growth in immature rats are (*a*) an inhibition of duct extension, (*b*) production of a small compact type of gland with thickened ducts and (*c*) pronounced development of the lobular-alveolar system.

JACOBSEN, Buffalo.

RELATION OF MAMMOGENIC LOBULE-ALVEOLAR GROWTH FACTOR OF THE ANTERIOR PITUITARY TO OTHER ANTERIOR PITUITARY HORMONES. J. P. MIXNER, A. J. BERGMAN and C. W. TURNER, Endocrinology **31**:461 (Oct.) 1942.

Comparative assays indicated that the mammogenic lobule-alveolar growth factor of the anterior lobe of the pituitary gland is not identical with the lactogenic, the thyrotropic or the gonadotropic hormone.

JACOBSEN, Buffalo.

THE USE OF INSULIN IN ITS VARIOUS FORMS IN THE TREATMENT OF DIABETES. ELLIOTT P. JOSLIN, Bull. New York Acad. Med. **18**:200 (March) 1942.

The various forms of insulin now on the market and their clinical application in selected cases are discussed. This is a summary of the latest developments in insulin therapy and should be read in the original.

JAHR, Omaha.

VITAMIN DEFICIENCIES IN DIABETIC CHILDREN. JULIAN M. FRESTON, New York State J. Med. **42**:1833 (Oct. 1) 1942.

A clinical and partial chemical study was made to determine whether vitamin deficiencies were present in 93 children in a camp for children with diabetes. Twenty-six and eight thenths per cent of those examined were thought to show physical evidence of vitamin deficiency. For 24 patients chemical determinations of the amounts of carotene, vitamin A and ascorbic acid in the blood plasma were made. The content of carotene was normal in all the children except 1, in whom it was elevated. The levels of vitamins A and C in the blood were low in 21 of the 24 children tested. There was evidence of correlation between deficiency in vitamins and the presence of poorly controlled diabetes. AIKMAN, Rochester, N. Y.

THE ELECTROCARDIOGRAM OF CUSHING'S SYNDROME. E. GARCIA CARRILLO, Rev. argent. de cardiol. **8**:401 (Feb.) 1942.

A 17 year old boy with Cushing's syndrome died of myocardial weakness and cerebral hemorrhage. His electrocardiogram showed a bifid R wave in lead II.

SANFORD, Chicago.

HYPOPHYSIAL DWARFING. S. MUZZO and H. MUNOZ, Rev. chilena de pediat. **13**:429 (May) 1942.

The authors report hypophysial dwarfism in 2 children, aged 6 and 8 years.

An extract of the anterior lobe of the hypophysis cerebri was the only remedy which produced any effect. The preparation was given parenterally following the ingestion by the patient of large doses by the oral route. The preparation is more efficacious near the onset of puberty.

The authors conclude, however, that all hypophysial preparations so far used are of doubtful efficacy and seldom appreciably influence or improve the condition.

SCHLUTZ, Chicago.

EXPERIMENTS ON DENTAL LESIONS OF GLANDULAR ORIGIN. ORMANDO O. TACHELLA COSTA, ARCADIO C. BARAÑAO and EVARISTO FRATANTORI, Rev. méd. latino-am. **28**:43 (Oct.) 1942.

Extirpation of the thyroid and parathyroid glands in young dogs provoked faulty implantation, defective enamelization, delayed eruption and hypoplasia of the teeth and extreme prognathism of the inferior mandible in some subjects.

DWYER, Kansas City, Mo.

A CASE OF DIABETES IN EARLY CHILDHOOD. J. F. MORANO BRANDI, Rev. Soc. pediat. de la Plata **3**:24 (Jan.-April) 1942.

The author gives a detailed case study of a 2 year old child with diabetes and comments on the general handling of patients with this condition. He feels that testosterone propionate is a useful adjunct to dietetic and insulin therapy.

HIGGINS, Boston.

DIABETES INSIPIDUS AND DIURESIS OF TEN LITERS IN A CHILD. J. F. MORANO BRANDI, Rev. Soc. pediat. de la Plata **3**:113 (Aug.) 1942.

Polyuria and polydipsia developed in a girl of 11 years during an acute fifteen day illness, in which fever, nocturnal delirium and frontal headache were the other symptoms. The water intake reached as high as 12 liters a day, with a corresponding excretion of urine. Her blood cholesterol was 261 mg. per hundred cubic centimeters. Treatment temporarily reduced the excretion to 5 liters. The cause of the condition was not otherwise explained than by the infection.

HIGGINS, Boston.

Diseases of the Muscles, Bones, Joints and Lymph Glands

A CASE OF DERMATOMYOSITIS. MURIEL J. L. FRAZER, Brit. J. Dermat. **54**:265 (Oct.) 1942.

A case of dermatomyositis is reported in which at autopsy the muscular lesions predominated, the cutaneous changes being relatively slight.

BLUEFARB, Chicago.
[ARCH. DERMAT. & SYPH.]

AMYOTONIA (MYATONIA) CONGENITA: OPPENHEIM'S DISEASE. G. B. HASSIN, J. Neuropath. & Exper. Neurol. **1**:351 (Oct.) 1942.

Hassin reports the clinical and pathologic changes in the case of a 6 month old Italian girl who presented the clinical picture of amyotonia congenita. She had had extreme weakness of the lower extremities since birth and was unable to sit up because of weakness of the muscles of the neck and back. The legs were motionless and extended but showed no atrophy. All tendon reflexes were absent. She died at the age of 7 months—the exact age at which a sibling had died of "paralysis."

Histologic examination of the spinal cord revealed scarcity of nerve cells throughout, especially in the lumbosacral region. Here some of the cells were reduced in size, appeared homogeneous and contained scant Nissl substance at the periphery. Occasional cells showed satellitosis and neuronophagia. A striking feature of the microscopic picture was the presence of numerous heterotopic nerve cells in the ventral portion of the spinal column, the posterior roots of the spinal nerves, the pia and the subarachnoid space. The white substance of the cord contained increased numbers of microgliocytes, oligodendrocytes and cytoplasmic astrocytes. There was less myelin in the pyramidal tracts, the posterior column, the lateral limiting zone and the ventral root zone than in the marginal areas, the spinocerebellar tracts and the ventral pyramid. The peripheral nerves appeared normal.

Microscopic study of muscle showed that in some bundles the fibers appeared normal, but in others there were hypoplastic muscle fibers interspersed with bundles of unripe embryonic fibers, and occasional hypertrophic fibers, some of which were in a state of regression.

Similar changes, confined to the "peripheral neuromuscular neuron" have been described in cases of Werdnig-Hoffmann disease (infantile progressive muscular atrophy). It is thought that in both diseases there is retarded development of the anterior horn cells, myelin sheaths and muscles. While Hassin feels that a differential diagnosis of either disease cannot be made from the microscopic appearance of the muscles or the spinal cord, it is noteworthy that the numerous heterotopic nerve cells observed in this case of amyotonia congenita have not been described in cases of Werdnig-Hoffmann disease.

CAMPBELL, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

BILATERAL CONGENITAL SUBLUXATION OF THE ACROMIOCLAVICULAR JOINT. JOHN GRIEVE, Lancet **2**:424 (Oct. 10) 1942.

Congenital dislocations and subluxations in the region of the shoulder are not common.

In the author's reports on 2 patients (men 18 and 20 years of age) the evidence of the congenital nature of these dislocations and subluxations is circumstantial, but neither patient had a history of antecedent trauma. The father of 1 of these men probably had a similar condition.

LANGMANN, New York.

THE ELECTROCARDIOGRAM IN FAMILIAL MUSCULAR DYSTROPHY. E. GARCIA CARRILLO, Rev. argent. de cardiol. **7**:122 (June) 1941.

The electrocardiograms of 2 of 3 children with myotonia showed abnormalities, including low voltage in the P wave, a prolonged PR interval, a wide and notched QRS complex and deviation of the axis to the left.

SANFORD, Chicago.

MULTIPLE PROGRESSIVE MYOSITIS OSSIFICANS: THE DISEASE OF MÜNCHMAYER. H. W. JAEGER, Rev. chilena de pediat. **13**:785 (Sept.) 1942.

Multiple progressive myositis ossificans, an extremely rare condition, was observed in a boy aged 5 years. When the child was 7 months of age small tumors were noticed in the neck and over the back in the scapulohumeral region. In time these tumors increased in number and invaded the upper extremities, the muscles used in mastication, the entire thorax and part of

the abdomen. Marked limitation of motion ensued. Walking and speech were difficult on account of immobilization of the inferior maxillary bone due to the tumors.

The mouth could hardly be opened. When the affected muscles were palpated, painless irregular hard bony masses were felt. The overlying skin was not changed and was not adherent to the osteomas.

The lower extremities were not involved except that there were hallux valgus and microdactylia of the large toes.

Roentgen examination showed numerous dense, bony shadows in the soft structures of the region of the neck, the axillas, the upper extremities, the trunk and the abdomen. In the last region the shadows showed branching formations. The femurs, tibia and os calcis showed symmetric exostitis. The humeri of both arms were markedly deformed, as were the costal arches on the right side. The distal extremity of the first metatarsal bone showed considerable deformity, and there was metatarsal phalangeal subluxation with marked agenesis of the second phalanx of both large toes.

Wassermann and Kahn tests gave negative results. The blood picture was normal. Phosphorus was 2.51 mg., calcium 11.9 mg. and phosphatase 2.7 Gm. per hundred cubic centimeters of blood. Biopsy showed the tumor masses to consist of cartilaginous and fibrous structure with extensive infiltration of bony tissue in various stages of development. Zones of hemorrhagic infiltration and subacute inflammation were also found.

There is no treatment for this excessively rare and deforming condition. It is literally a living petrification. It is not a familial or a hereditary disease.

SCHLUTZ, Chicago.

SOLITARY CHONDROMAS AND CHONDROMATOSIS. R. E. MILLAN, Rev. Soc. pediat. de La Plata **3**:219 (Nov.) 1942.

A girl of 8 years had had for two years pain, at times severe, in the right hip and claudication in the right leg on walking. A tumor was detected on the right ischiopubic ramus by rectal examination and by roentgenography. The tumor was removed, and microscopic examination confirmed the diagnosis of benign chondroma. Pressure on branches of the obturator nerve explained the symptoms. HIGGINS, Boston.

BONE CYST. EUGENIO TRAVELLA, Rev. Soc. pediat. de Rosario **7**:3 (Jan.-April) 1942.

Travella describes a case of bone cyst and its treatment. LOZOYA S., Mexico, Mexico.

A CASE OF STILL'S (MULTIPLE RHEUMATOID ARTHRITIS) DISEASE. J. F. MORANO BRANDI, Rev. Soc. pediat. de la Plata **3**:66 (Jan.-April) 1942.

A boy of 2 years with multiple rheumatoid arthritis recovered from an exacerbation of that condition almost immediately after tonsillectomy and adenoidectomy. He had been sick for ten months. This relief is no assurance against a recurrence of the condition.

HIGGINS, Boston.

OSTEOMYELITIS OF THE SUPERIOR MAXILLA IN AN INFANT. JOSE CELORIA, Rev. Soc. pediat. de Rosario **7**:9 (Jan.-April) 1942.

Celoria describes a case in which osteomyelitis of both superior maxillas in a baby 7 months old was successfully treated surgically.

LOZOYA S., Mexico, Mexico.

Diseases of the Eye

OPERATION FOR CONGENITAL GLAUCOMA. O. BARKAN, Am. J. Ophth. **25**:552 (May) 1942.

Barkan presents the following summary and conclusions:

"In this paper the results of operations on 17 eyes with congenital glaucoma are reported. Pressure was normalized in 16 of the 17 eyes; visual function was maintained in 14. Of the 3 blind eyes brought to operation, vision was lost in 2 before surgery was instituted. In only 1 case did operation fail to normalize the pressure in time to save vision. Sight was preserved in the fellow eyes of these three infants so that they were saved from blindness. The average age at time of operation was three months. From one to five years have elapsed since the operations were performed. On the basis of the successful results and of pre- and postoperative gonioscopy, certain conclusions are arrived at in regard to the underlying pathology and to the mode of action of the operation. It appears that the majority, if not all, binocular cases of congenital glaucoma are due to a developmental obstruction in the excretory angle which, when removed, permits outflow of aqueous into the canal of Schlemm. The canal is found to be present and ready to function in the large majority of cases in which the diagnosis is made at a sufficiently early age, before prolonged distention of the eyeball has obliterated the canal. Early diagnosis and early operation are therefore urgently indicated. The operation gives a high promise of permanent success with a remarkable degree of safety and without disfigurement."

REESE, Philadelphia. [ARCH. OPHTH.]

ANOMALOUS PROCESSES OF CILIARY TYPE ON POSTERIOR SURFACE OF IRIS. S. GARTNER, Am. J. Ophth. **25**: 854 (July) 1942.

Gartner gives the following summary:

"Twenty-six cases are reported of anomalous processes on the posterior surface of the iris. They closely resemble the ciliary processes, from which they are separated by normal iris tissue. The anomalous processes are fetal remains of tissue which usually disappear by the time of birth. Their presence can assume practical importance in complicating an iridectomy, inasmuch as they may cause increased hemorrhage and postoperative reaction."

REESE, Philadelphia. [ARCH. OPHTH.]

DISPLACEMENT OF CILIARY PROCESSES TO POSTERIOR SURFACE OF IRIS. S. GARTNER, Am. J. Ophth. **25**: 858 (July) 1942.

Gartner gives the following summary:

"Partial displacement of ciliary processes to the posterior surface of the iris is a common variation from the normal. This is explained by the embryology of the ciliary processes. Its importance in iridectomy is discussed." REESE, Philadelphia. [ARCH. OPHTH.]

ANGIOID STREAKING OF THE RETINA. L. LEHRFELD and S. S. BRAV, Am. J. Ophth. **25**:1222 (Oct.) 1942.

Lehrfeld and Brav report 2 cases of angioid streaks of the retina associated with pseudoxanthoma elasticum in sisters. REESE, Philadelphia. [ARCH. OPHTH.]

NODULAR KERATITIS. O. H. ELLIS, Am. J. Ophth. **25**: 1224 (Oct.) 1942.

Ellis reports a case of nodular keratitis observed from its incipiency. The patient's mother, 2 aunts, 2 sisters, a niece and probably her paternal great-grandfather all suffered from the condition. Surgical treatment did not improve the vision. Since the condition

began with the onset of the menses and the pain ceased during two pregnancies, Ellis feels that it may have been due to an endocrine imbalance.

REESE, Philadelphia. [ARCH. OPHTH.]

BOUQUET-NÈGRE ANTIGEN AND ITS USE IN THE TREATMENT OF PHLYCTENULAR KERATOCONJUNCTIVITIS. FLAVIO LOMBARDI, Arch. de pediat. **14**:158 (Feb.) 1942.

The author describes the technic for the preparation of the methylic antigen of Bouquet and Nègre (triturated dried tubercle bacilli in acetone and methyl alcohol). He is impressed by its action in the treatment of phlyctenular keratoconjunctivitis.

LOZOYA S., Mexico, Mexico.

ANGIOMATOSIS RETINAE (VON HIPPEL-LINDAU DISEASE): REPORT ON A GENEALOGIC TREE. W. RUMBAUR, Klin. Monatsbl. f. Augenh. **106**:168 (Feb.) 1941.

Five members of a family presented symptoms of angiomatosis of the retina. Six of 15 other members of the same family had anomalies of other parts of the body, such as tumor of the pancreas, complicated by angiomatosis retinae in 1 case and by diabetes in another, and 1 had a tumor of the brain. Three other members had lesions of an allied nature: One had juvenile presclerosis with retinal angiomatosis; 1, coloboma of the iris, microphthalmos and defective speech, and another, microcephalus and idiocy. Members of four generations were examined.

The first 5 patients mentioned presented angiomatosis of the retina in different stages, varying from the prodromal phase without angiomatous nodules in 1 patient to partial degeneration of the retina with rapid decrease of function in another. The last-named patient was the second to present the nodule behind the retina.

In the fifth patient recovery occurred in one eye but in the other the process terminated in detachment of the retina. The case is proof of the synchronous occurrence in the same patient of the benign form of the disease in one eye and of the malignant form in the other. The condition, furthermore, was complicated by an adenoma of the pancreas; the tumor had remained without recurrence for fifteen years, after having been reduced in size by removal of a specimen for biopsy.

Observation of the patients led Rumbaur to express the belief that the vascular changes are primary and that the angiomatous nodules form secondarily at the junction, or anastomosis, of arteries and diseased veins. So-called isolated angiomatous nodules arise from fine capillaries, which cannot be observed with the ophthalmoscope; they may be enlarged capillaroglomeruli, as described by Czermak, von Hippel and other investigators.

In the fourth patient the retinal angiomatosis healed spontaneously. The fifth patient may have had a similar recovery in the one eye, for "empty," pale nodules were observed. Their presence permits the conclusion that the prognosis of retinal angiomatosis is not always unfavorable. The von Hippel-Lindau syndrome is due to specific hereditary factors.

The author undertook treatment of some of his patients, a satisfactory result being obtained with diathermy in some instances. In 1 patient he attacked the nodule directly with the diathermy needle, destroying it with coagulation. He produced healing of numerous secondary changes in the retina by coagulation of a large angiomatous nodule. In this manner the tumor could be reduced in size by operation and smaller nodules be made to disappear.

STOLL, Cincinnati. [ARCH. OPHTH.]

Skin Diseases; Allergy

ERYTHEMA NODOSUM. M. H. POPPEL and A. M. MELAMED, New England J. Med. **227**:325 (Aug. 27) 1942.

Erythema nodosum is three to five times more prevalent in females than in males and is most frequent in young persons. It is rare in children under the age of 3 years and in old persons. It is most prevalent during the spring season. Wallgren has shown that in Scandinavian children 95 per cent of the cases of erythema nodosum appear with tuberculosis; in England this percentage is 70, and in the United States it is lower. He stated the belief that in tuberculous children the erythema nodosum appears when the child becomes sensitive to tuberculin.

In this series of 88 cases, the condition was three times more prevalent in females; the ages of the patients ranged from 2 to 58 years. Of the 44 tuberculin tests that were performed on half the patients, 33 gave positive results. Roentgenograms of the chest were available in 56 of the 88 cases. Fourteen of these showed pulmonary changes or enlargement of the intrathoracic lymph nodes or both.

In a small group of patients (approximately 15 per cent), no evident associated disease was present. The following conditions were most frequently associated with the erythema nodosum in these 88 cases: tuberculosis (4 cases); rheumatic heart disease (7 definite and 10 questionable cases); ulcerative colitis (6 cases); infections of the upper respiratory tract (49 cases); arthralgias (28 cases); ingestion of a drug (8 cases); inactive syphilis (4 cases); gonorrhea (4 cases).

GENGENBACH, Denver.

MOLES AND MALFORMATIONS OF THE SKIN. E. MEIROWSKY, Brit. J. Dermat. **54**:99 (April); 129 (May) 1942.

Man has become prone to have nevi and malformations of the skin by the factors of both domestication and phylogenesis. By the process of domestication new mutations have arisen in the germ plasm, producing general and circumscribed genodermatoses. Nevi are inherited and determined to the extent of nine tenths by the germ plasm. The unilateral formation of nevi is conditioned by the fact that genes can become effective only on one side of the body. The locations in which nevi appear are determined by the regions which have played their part in the phylogenetic development (regions of clefts, of the spine, of the nipple, of sinus hairs and of markings of animal and human piebalds). All experimental and clinical investigations confirm the results of the analysis of normal skin; the germ plasm governs both its normal and its abnormal development. That is the elementary point from which research on moles must be continued.

BLUEFARB, Chicago. [ARCH. DERMAT. & SYPH.]

A CASE OF PROBABLE IDIOSYNCRASY TO HUMAN MILK. FLAVIO LOMBARDI, Arch. de pediat. **14**:131 (Jan.) 1942.

A 10 day old baby with diarrhea, treated by all common methods, became worse and finally presented all the symptoms of intoxication. The child was cured

immediately when all human milk was withheld and a powdered dried milk with some of the fat removed (Dryco) was substituted.

Lozoya S., Mexico, Mexico.

Surgery and Orthopedics

Treatment of Femoral Shaft Fractures in Infants. Henry Milch, M. Rec. **155**:360 (July) 1942.

A practical apparatus is described for the treatment of fractures of the femoral shaft when hospitalization and overhead traction are not possible. It consists of a plaster of paris trunk cast, with an incorporated steel bar which is bent to the proper shape and extended beyond the foot. Elastic traction is applied by attaching the extremity (which has been prepared in the usual manner) to a hook at the end of the steel bar, by means of rubber bands or rubber tubing. The cases of 3 patients treated satisfactorily in this manner are reviewed. Pictures are included.

Ferdinand, Peoria, Ill.

A Practicable Outline for the Treatment of Burns. Donald W. MacCollum, New England J. Med. **227**:331 (Aug. 27) 1942.

In this article a general survey of the treatment of burns has been outlined in detail, with particular emphasis on the treatment of shock, the need for gentleness in the handling of tissues and the necessity for a complete cleansing of the burned area before medicaments are applied. All types of burns are discussed, including thermal (hot liquids, steam, flame and hot metals), chemical and electrical burns.

Gengenbach, Denver.

Teeth and Dentistry

Finger-Sucking: Serial Dental Study from Birth to Five Years. J. H. Stillman, New York State J. Med. **42**:2024 (Nov. 1) 1942.

A dental study was made of over 1,000 newborn children. Models were made of the gum pads of 200 of these infants. Irregularities of the deciduous teeth are common, regardless of habit, and rotations may be present even before eruption. Small children have the physiologic urge to bite on the overlying gum, the fingers or various other objects. Heckling the child is often responsible for turning the physiologic sucking and biting into a habit. In most instances in which crooked teeth have been caused by sucking, correction is spontaneous. At least, a finger sucker must breathe through his nose and not through his mouth.

Aikman, Rochester, N. Y.

The Importance of Orthodontia in Pediatrics. A. C. Miranda, Rev. Soc. pediat. de la Plata **3**:163 (Aug.) 1942.

Orthodontia will prevent the consequences of improper mastication, diminish caries and pyorrhea, prevent abnormalities of the nasal passages and sinuses, improve the esthetic appearance and correct difficulties of phonation.

Higgins, Boston.

Miscellaneous

Vibration of the Thorax by Percussion of the Skull and Patella. E. Correa de Azevedo, Arch. de pediat. **14**:206 (March) 1942.

Percussion of the patella is transmitted by the femur, the iliac bones and the vertebrae to the thorax, and the vibrations then follow the ribs and intercostal spaces. A similar sequence of transmissions occurs if the skull is percussed. Anything that hinders the vibration of the thoracic case can be demonstrated by this technic.

Lozoya S., Mexico, Mexico.

The Antepartum Examination. Domingos F. Machado, Pediat. e puericult. **11**:51 (Sept.-Dec.) 1941.

The author insists on the importance of a good antepartum examination with special emphasis on pelvicephalometry as described by Ball.

Lozoya S., Mexico, Mexico.

Sulfadiazine. Samuel Morones, Prensa med. mex. **7**:73 (June 15) 1942.

Morones reports on 178 cases of pneumococcic pneumonia in which sulfadiazine was used; the mortality was 10.7 per cent. In 687 cases in which sulfapyridine was used the mortality was 16.3 per cent. In 138 cases of nonpneumococcic pneumonia (streptococcic staphylococcic, etc.) the mortality was 21 per cent, while in those in which sulfathiazole was used the mortality was 23 per cent. The first dose of sulfathiazole as well as of sulfadiazine was 4 Gm. and then 1 Gm. was given every four hours (reduced for children in proportion). In 460 cases in which there were nausea and vomiting sulfadiazine was tolerated well. In 35 cases the urine showed crystals, and in only 1 was there renal colic and hematuria. Comparing the toxic effect of sulfapyridine with that of sulfadiazine the results were as follows: Of 66 patients taking sulfathiazole, 39 had vomiting, hematuria and dermatitis; of those taking sulfadiazine, 13 had minor disturbances.

Giffen, Toledo, Ohio.

Therapeutics of Sulfonamide Compounds: The Importance of Study of Their Concentration in the Body. R. C. Aguirre, J. R. Calcarami and H. M. Berisso, Rev. chilena de pediat. **13**:167 (Feb.-March) 1942.

The authors conclude that it is of greatest practical importance to know the concentration of administered sulfonamide compounds in the various fluids of the body. This is necessary not only for an appreciation of their therapeutic value but for recognition of toxic symptoms. It is only by this knowledge that one can decide on adequate dosage.

In general a direct relationship was found between the doses given and the concentrations of the drug in the blood. It varied somewhat according to the sulfonamide compound employed. The greatest concentration after a single dose per kilogram of body weight was found after the use of sulfanilamide. The concentration of the drug in the blood was greater with sulfanilamide than with sulfapyridine and sulfathiazole.

For the infant, higher doses per kilogram of body weight must be given than for the adult in order to have effective concentrations of the drug in the blood. The infant has a greater renal capacity for excretion of the drug than has the adult.

The therapeutic action of this medication is achieved through the medium of the most effective concentration in the blood. This concentration must be maintained fairly constantly for several days. Some patients have good therapeutic results with low concentrations of the drug in the blood, even as low as 1 or 2 mg. per hundred cubic centimeters. The authors have had therapeutic failure with levels as high as 8 and 15 mg. per hundred cubic centimeters.

Toxic symptoms occur if there is a special sensitivity of the organism. The majority of the conditions of

intolerance have a distinct relation to the levels of the drugs in the blood and to the prolonged use of the drugs in the treatment.

With the use of isotonic solution of sodium chloride by rectal and intravenous route, optimal blood concentrations of the drugs can be readily maintained. Medication should be by this route if there is marked gastric intolerance to a sulfonamide compound or if the patient is in a state of coma. The authors do not report strikingly favorable results in various forms of meningitis and attribute this to the low permeability of the meninges to this type of medication. The concentration of a sulfonamide compound in the cerebrospinal fluid is always lower than the concentration in the blood—sometimes 23 per cent lower with sulfanilamide, 36 per cent with sulfapyridine and 60 to 80 per cent with sulfathiazole.

Introduction of the drug into the cisterna and directly into the cerebrospinal canal will sometimes give good concentrations, comparable to those in the blood. For the various purulent forms of meningitis the concentration of the drug in the spinal fluid should be between 10 and 50 mg. per hundred cubic centimeters of blood. The concentration in the pleural fluid is generally 25 per cent lower than that in the blood.

The drugs can be given by the intrapleural route in cases of purulent pleurisy.

Sulfonamide compounds circulating in the organism are eliminated in the urine in two forms, free and conjugated. The proportion of the direct circulation of the conjugated form as related to the total in the blood is as follows: sulfanilamide 17 per cent, sulfapyridine 43 per cent and sulfathiazole 21 per cent. In the urine, sulfanilamide shows 45 per cent, sulfapyridine 58 per cent and sulfathiazole 47 per cent of the conjugated form.

The knowledge of the concentration of the sulfonamide compounds in the urine is important in the treatment of urinary infections. Patients treated usually responded rapidly to concentrations which varied between 80 and 265 mg. per hundred cubic centimeters of blood of the free sulfonamide compound.

Sulfonamide compounds are eliminated almost entirely in the urine. There exists an equilibrium between the amount ingested and the amount excreted. The drug does not usually accumulate in the organism. The quantity of liquid consumed has an important bearing on the degree of elimination. Diminution of diuresis causes an increase of the drug in the blood and in the urine, but the quantity excreted per day may be diminished. Administration of large amounts of fluids has a contrary effect. In case of renal insufficiency the diminution of excretion of the sulfonamide compound from the urine is in proportion to its concentration in the blood. The accumulation which may ensue can become dangerous.

SCHLUTZ, Chicago.

SUDDEN DEATH IN INFANCY. J. D. LUQUE, Rev. chilena de pediat. **13**:659 (July) 1942.

The infants who die suddenly are usually of one of two types: One includes fat, pasty-appearing babies with generalized enlargement of the lymphatic structures, including the thymus and, in some instances, with eczema; the other type includes those affected with latent or manifest spasmophilia. In the first type, an allergic response precipitates the conditions which lead to sudden death.

SCHLUTZ, Chicago.

SULFONAMIDE THERAPY IN INFANCY. M. J. DEL CARRILL, G. FOLEY, A. LARGUIA and E. SOJO, Rev. chilena de pediat. **13**:701 (Aug.) 1942.

The authors give an excellent review of the most acceptable theories concerning the action of these drugs and also of the explanation of the toxic effects which occasionally ensue in the course of their use. On the basis of extensive case material, the clinical use of the drugs is illustrated.

In using one of them in an infant, one must consider the gravity of the infection, the tolerance to the drug at this age level and the condition of the infant.

The authors consider as a minimal dose for infants of 1 year 0.1 Gm. per kilogram of body weight in twenty-four hours, and as maximal dose, 0.3 to 0.4 Gm. A fractional dose of sulfanilamide or sulfapyridine is given every six hours and of sulfathiazole every four hours. The initial dose of all preparations must always be larger than any subsequent dose, in order to obtain an adequate level of the sulfonamide compound in the blood as quickly as possible.

SCHLUTZ, Chicago.

Book Reviews

Allergy, Anaphylaxis and Immunotherapy. By Bret Ratner, M.D. Price, $8.50. Pp. 834, with 88 illustrations and 56 tables. Baltimore: The Williams and Wilkins Company, 1943.

This book is defined by its author as "a treatise presenting the fundamental principles and practice governing the use of antisera, vaccines, toxoids, blood transfusions, blood substitutes and sulfonamides in the treatment of infectious diseases and of the allergic phenomena resulting from their use."

It is divided into three parts, as follows: "Immunotherapy," 359 pages; "Allergy to Immunotherapeutic Agents," 215 pages, and "The Allergic State," 209 pages.

The first part begins with a discussion of the nature and preparation of the various serums used in treating the infectious diseases, and includes 48 pages on treatment with sulfonamide compounds; then it goes on to a complete consideration of both the theoretic and the practical aspects of the prophylaxis and treatment of all infectious diseases by means of biologic agents.

The second part is concerned mostly with a discussion of serum sickness and serum allergy, and the third part contains a critical review of the fundamental principles underlying artificially induced sensitization.

This is not just another book; it is an important book. It is, in fact, unique. There is much meat in it, well presented and well arranged, with more thorough discussions of some subjects than can be found anywhere else. For example, 144 pages are devoted to a splendid presentation, both theoretic and practical, of serum sickness and serum allergy. It is, in the reviewer's opinion, the best discussion of this subject in print. That portion of the book devoted to immunotherapy for infectious diseases is particularly valuable to the pediatrician and accumulates from a large number of sources all the worth while information on the subject. The last part of the book is a critical review of the "allergic state" from the viewpoint of artificially induced allergy. There is little about naturally occurring human allergy in the book; it is therefore not a textbook for allergists. The author does not pretend that it is and specifically states that he is discussing the allergic phenomena resulting from the use of antiserums, vaccines, toxoids, blood transfusions, blood substitutes and sulfonamide compounds. The title should be "Immunotherapy, Anaphylaxis and Allergy."

Dr. Ratner has written a magnificent book, different in scope from any other available. It should be owned by every one who wishes to understand the modern treatment of infectious diseases.

Brucellosis in Man and Animals. Revised edition. By I. Forest Huddleson, D.V.M., M.S., Ph.D. Contributing authors, Dr. A. V. Hardy, Dr. J. S. DeBono and Dr. Ward Giltner. Price, $3.50. Pp. 379, with 42 illustrations. New York: The Commonwealth Fund, 1943.

The second edition of "Brucellosis in Man and Animals" deserves the careful attention of clinician, laboratory worker and veterinarian. Dr. Huddleson, as research professor of bacteriology at Michigan State College, has spent a great deal of his time on the subject and has himself made studies of the conditions on the island of Malta as well as in this country. The contributing authors are also established authorities. Dr. DeBono is professor of pharmacology and therapeutics at the Royal University of Malta. Dr. Hardy is associate professor of epidemiology at Columbia University College of Physicians and Surgeons, and Dr. Giltner is dean of the veterinary division and professor of bacteriology at Michigan State College.

The details of laboratory procedure and the problems which may be encountered in establishing a diagnosis by this means should not be overlooked by the clinician, for it is by his knowledge of what tests to ask for and how to interpret the results that the diagnosis of brucellosis can be made. The excellent manner in which these problems are presented makes this an interesting task. The new edition has full descriptions of the dissociated types of organisms and gives a good discussion of a method for determining virulence. The account of clinical aspects of the disease, with numerous case reports, is extremely valuable in that it puts one on the watch for possible instances of this condition and suggests methods of treatment. The discussion of the disease as it occurs in animals gives one an appreciation of the epidemiologic aspects and problems of eradication or control.

Your First Baby. By Louise Cripps Glemser. Price, $1.00. Pp. 90, with 14 illustrations. New York: A. S. Barnes and Company, 1943.

The humor and good sense with which this book is written will prove a boon to many a mother confronted with her first baby. The information is excellent, based on an understanding of the needs and the development of the infant and also on the needs of the mother for reassurance and relaxation. The illustrations are delightful. Ample space for photographs is provided in the part of the book set aside for the individual baby's record.

Directory of Pediatric Societies *

INTERNATIONAL

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Place: Boston. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

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President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340,'s Gravenhage.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialkstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

Sociedad Cubana de Pediatria

President: Dr. Angel A. Aballí Arellano, 17 No. 609 Vedado, Habana.
Secretary: Dr. Julio G. Cabrera Calderin, Hospital Mercedes L y 21 (Vedado), Box 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Sociedad Mexicana de Pediatria

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. E. Santos Mendoza.
Secretary: Dr. P. Oropeza, Hospital de Niños, Caracas.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincare, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Uruguyan Society of Pediatrics

President: Dr. Nicolas Leone Bloise, Avenida Agraciada 2496, Montevideo.
Secretary: Dr. Héctor Mourigan, Avenida Agraciada 1464, Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 315 Alameda Rd., Kansas City, Mo.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: Chicago. Time: June 12-16, 1944.

American Academy of Pediatrics

President: Dr. Franklin P. Gengenbach, 1850 Gilpin St., Denver, Colo.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: St. Louis, Mo. Time: Feb. 10-12, 1944.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

American Hospital Association, Children's Hospital Section

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

American Pediatric Society

President: Dr. James L. Gamble, 300 Longwood Ave., Boston, Mass.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. Struthers, 906 Drummond Medical Bldg., Montreal.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. Joseph A. Johnston, Henry Ford Hospital, Detroit.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. Warren R. Sisson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

Northwestern Pediatric Society

President: Dr. Arild E. Hansen, University of Minnesota, Minneapolis.
Secretary-Treasurer: Dr. Albert V. Stoesser, 205 W. University Hospital, Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary. Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

Alabama Pediatric Society

President: Dr. Amas Gipson, 948 Forrest Ave., Gadsen.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. William C. Deamer, University of California Hospital, San Francisco.
Secretary: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco.

Florida State Pediatric Society

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. T. F. Davenport, 104 Ponce de Leon Ave. N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. A. Clement Silverman, 608 E. Genesee St., Syracuse.
Secretary: Dr. Albert G. Davis, 307 Gas and Electric Bldg., Utica.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Charles F. McKhann, University Hospital, Ann Arbor.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. E. W. Hancock, 820 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. John M. Thomas, 1102 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NEW HAMPSHIRE PEDIATRIC SOCIETY

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Thomas M. Watson, Greenville.
Secretary: Dr. Frederick B. Haar, Greenville.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Ben H. Nicholson, 301 N. W. 12th St., Oklahoma City.
Secretary: Dr. Luvern Hays, 108 W. 6th St., Tulsa.
Place: Oklahoma Club. Time: 6:30 p. m., fourth Friday of each alternate month from September to May, inclusive.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, Wade Hampton Office Bldg., Columbia.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Edwin A. Harper, 301 Rivermont Ave., Lynchburg.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND PEDIATRIC SECTION

Chairman: Dr. J. D. Nourse, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. I. B. Silber, 10465 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. I. Nelles Silverthorne, 170 St. George St., Toronto, Canada.
Secretary: Dr. G. P. Hamblin, 2333 Bloor St. W., Toronto, Canada.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry J. Cohen, 1975 Walton Ave., New York.
Secretary: Dr. Walter Levy, 12 E. 88th St., New York.
Place: Concourse Plaza Hotel, 161st St., and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Harry A. Naumer, 37–8th Ave., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Granada Hotel. Time: Fourth Wednesday of October, November, February, March and April.

BUFFALO PEDIATRIC SOCIETY

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Edward J. Wynkoop, 501 James St., Syracuse.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places:: Various cities in New York. Time: Third Tuesday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Heyworth N. Sanford, 952 N. Michigan Ave., Chicago.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, Inclusive.

Cincinnati Pediatric Society

President: Dr. Lloyd K. Felter, 3144 Jefferson Ave., Cincinnati.
Secretary: Dr. T. Selkirk, 3530 Reading Rd., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Belfort, Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Hugh Lewis, Detroit, Mich.
Secretary: Dr. John J. Pollack, 622-26 Maccabees Bldg., Detroit, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatrics Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Bikoff, 850 St. Marks Ave., Brooklyn.
Secretary: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month, October to April, inclusive.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Woodley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. John H. Reynolds, 1628 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. F. J. Mellencamp, 324 E. Wisconsin Ave., Milwaukee.
Place: Milwaukee Athletic Club. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Edith M. Lincoln, 600 Park Ave., New York.
Secretary: Dr. John D. Lyttle, Babies Hospital, New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Affiliates

President: Dr. Crawford Bost, 490 Post St., San Francisco.
Secretary: Dr. William A. Reilly, 384 Post St., San Francisco.
Time: Second Thursday of September, November, January, March and May.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 625 N. W. 10th St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Theodore S. Wilder, Greene and Coulter Sts., Germantown, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday in March, May, October and December.

Pittsburgh Pediatric Society

President: Dr. Carl Ruder, 646 Washington Rd., Mount Lebanon, Pittsburgh.

Secretary-Treasurer: Dr. C. J. Stoecklein, 125 De Soto St., Pittsburgh.

Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate month from October to June, inclusive.

Richmond Pediatric Society

President: Dr. Stanley Meade, 913 Floyd Ave., Richmond, Va.

Secretary-Treasurer: Dr. Louise Galvin, 214 S. Boulevard, Richmond, Va.

Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. Herbert Soule, 122 Rutgers St., Rochester, N. Y.

Secretary-Treasurer: Dr. Jerome Glaser, 300 S. Goodman St., Rochester, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Jerome Diamond, 508 N. Grand Ave., St. Louis.

Secretary-Treasurer: Dr. Mary A. McLoon, 408 Humboldt Bldg., St. Louis.

Place: St. Louis Medical Society Bldg. Time: First Friday of each month from November to June.

Seattle Pediatric Society

President: Dr. Frederick B. Joy, Stimson Bldg., Seattle.

Secretary: Dr. Sherod M. Billington, Medical Dental Bldg., Seattle.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Jeanette Harrison, 1136 W. 6th St., Los Angeles.

Secretary: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.

Place: Jonathan Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Campbell Harvey, 35 W. Huron St., Pontiac, Mich.

Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.